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INTESTINAL INTOXICATION IN INFANTS

THE IMPORTANCE OF IMPAIRED RENAL FUNCTION *

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Preceding the development of toxic symptoms in intestinal intoxication[1] there is pronounced diarrhea, vomiting and diminished ingestion of fluid, the relative importance of which varies in different cases. In the acute stage of the symptoms the excretion of urine is greatly diminished, and at this time the urine contains albumin and abundant casts.

During the past year investigation of cases of intestinal intoxication has furnished evidence which emphasizes the importance of the loss of fluid and the impaired secretion of urine. In this communication it is proposed to present such evidence and to discuss its significance with special reference to the symptomatology.

I. NONPROTEIN NITROGEN AND UREA OF THE BLOOD

Technic.[2]—The nonprotein nitrogen was determined by the method of Gettler and Baker[3] except that the final determination was by aeration instead of by distillation. Fiftieth-normal acid and hundredth-normal alkali were used with methyl red as indicator. It was found that the presence of mercury used

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1. It is realized that the use of the term "intestinal intoxication" is open to objections. This term is not applied to the complex described by Finkelstein as "alimentäre intoxikätion" but is used merely to designate the series of toxic symptoms which frequently occur in association with profound nutritional disorders in infants.

The term "diarrhea with toxic symptoms" is cumbersome and is not more exact, for there is not always a direct relation between the severity of the diarrhea and the degree of toxemia. Indeed, there are cases with symptoms indistinguishable from those of intestinal intoxication in which there is no diarrhea at all.

2. All blood for analysis was withdrawn from the superior longitudinal sinus by means of a syringe and the type of needle described in a previous communication. The blood was always taken at least three hours after the last meal.

3. Gettler, A. O., and Baker, W.: Jour. Biol. Chem., 1916, **25**, 211.

in the precipitation of the protein interfered with the aeration of ammonia, probably through the formation of a stable ammonia-mercury compound which was not broken up by alkali. At Dr. Gettler's suggestion potassium hydrogen sulphid was used to precipitate the mercury, and by this means the obstacle was overcome. A very strong pump was used for aeration and blank determinations demonstrated that aeration for one half hour was sufficient. This was shown, (1) by determinations of pure ammonium sulphate or urea, and (2) by distilling mixtures which had been aerated from ten to thirty minutes to determine whether all ammonia had been removed.

As a rule 3 c.c. of blood were used. In some cases in which the nonprotein nitrogen was increased, the determination was made with only 2 c.c. In the earlier cases all determinations were made in duplicate. These were always within the limits of experimental error, and owing to the limited amount of blood one can take from infants, duplicates were omitted in the later cases. The purity of all reagents was checked by blank determinations. Whenever ammonia was present the amount was regularly deducted.

Urea was determined by the urease method of Van Slyke and Cullen.[4] The enzyme was tested for ureolytic power and also to exclude the presence of ammonia. Fiftieth-normal acid and hundredth-normal alkali were used with methyl red as indicator.

Normal Infants.—Determinations were made on thirty normal infants. Such infants were of practically normal weight, had normal appetite and bowel movements and were apparently well. The values for urea and nonprotein nitrogen are shown in Table 1.

In such infants the nonprotein nitrogen ranged from 23 to 39.1 mg. per 100 c.c. of blood. These figures are considerably higher than those obtained by Minsk and Sauer,[5] who used Folin's method. The difference is probably due to the difference in methods, as the values for normal adults obtained by Gettler and Baker are higher than those given by Folin's method.

The urea nitrogen was from 4.9 to 14.6 mg. per 100 c.c. of blood. In only a few cases was the urea nitrogen approximately one half of the nonprotein nitrogen, which is generally the case in adults and is what Minsk and Sauer[5] found in their patients. The difference in these results and those of Minsk and Sauer is due mainly to the fact that the values for nonprotein nitrogen were greater than theirs and not to the difference in the amounts of urea nitrogen.

As shown in Table 1, the amount of urea nitrogen varies greatly in different infants. A careful analysis of the food and the method of feeding fails to reveal an adequate cause for this variation. It seems possible that such variation may be due to the different rate of urea elimination by the kidney in accordance with Ambard's hypothesis.

Infants with Intestinal Intoxication.—Forty-six patients with intestinal intoxication were studied. Thirty-six had acidosis and thirty-three of these showed an increase in the nonprotein nitrogen of the blood. There were, therefore, only three patients with acidosis without

4. Van Slyke, D. D., and Cullen, G. E.: Jour. Am. Med. Assn., 1914 **62**, 1558.
5. Minsk, L. D., and Sauer, L. W.: Am. Jour. Dis. Child., 1917, **13**, 397.

TABLE 1.—The Nonprotein Nitrogen and Urea Nitrogen in the Blood of Normal Infants *

Number	Age, Months	Weight		Carbon Dioxid Tension Alveolar Air, Mm.	Nonprotein Nitrogen, Mg. per 100 C.c. of Blood	Urea Nitrogen, Mg. per 100 C.c. of Blood
		Lb.	Oz.			
1	1¼	9	4	38.2	33.35	8.6
2	1½	9	1	36.6	35.1	7.4
3	1¾	9	2	41.2	30.15	13.8
4	2¼	10	1	39.1	34.0	12.9
5	2½	10	4	42.4	35.2	10.3
6	3	11	4	40.6	37.6	4.9
7	3¼	11	4	37.6	39.1	7.7
8	3¾	11	8	35.9	36.2	13.3
9	3¾	11	4	38.7	38.0	11.8
10	4	12		41.2	39.1	10.9
11	4½	12	4	40.1	35.2	12.2
12	4½	11	12	36.1	35.4	12.3
13	4¾	13	12	40.0	39.0	11.3
14	5¼	14	1	39.1	27.6	8.3
15	5½	13	4	36.8	29.8	11.2
16	5¾	12	15	40.1	38.2	7.1
17	5¾	14	14	44.6	26.6	8.3
18	6	15	8	37.8	27.4	14.6
19	6½	15	14	43.2	34.3	13.9
20	7	18	4	35.8	31.1	7.9
21	7¼	17	2	39.2	38.0	11.8
22	7½	16	12	40.3	24.2	11.7
23	7½	17	4	41.2	23.0	7.8
24	8¼	17	12	36.7	31.6	10.7
25	9	18		38.9	27.5	4.9
26	9½	18	14	37.6	25.0	10.2
27	10	17	14	42.3	38.4	11.3
28	11	21	11	36.4	34.3	10.1
29	11¾	20	4	40.1	31.2	7.2
30	12	21	4	37.5	28.0	9.3

* The air was collected by the Plesch-Higgins method as modified by Howland and Marriott. The air analyses were made in the Haldane apparatus.

an increase of the nonprotein nitrogen. In only one of these patients was more than one determination made. There were four cases without acidosis but with an increased nonprotein nitrogen and four cases with neither acidosis nor increased nonprotein nitrogen. Thirty-seven of the forty-six cases showed a decided increase in the nonprotein nitrogen of the blood.

Twenty-three of the cases with acidosis are shown in Table 2. These were selected for presentation as they were the ones most completely observed, and, moreover, they are representative of the entire series. Of these cases there was only one with no increase in the nonprotein nitrogen (Case 18). In the remainder the nonprotein nitrogen ranged from 57 to 232 mg. per 100 c.c. of blood, the urea nitrogen from 20.1 mg. to 108.2 mg. per 100 c.c. of blood. Comparison with the results from normal infants (Table 1) shows that in intestinal intoxication the urea and nonprotein nitrogen are much increased.

Minsk and Sauer[5] determined the nonprotein and urea nitrogen in six cases of intestinal intoxication; in three there was a distinct increase. The greatest nonprotein nitrogen in their cases was 67.6 mg. nitrogen per 100 c.c. of blood, which was much lower than in most of my cases. The urea nitrogen in their cases constituted a larger percentage of the nonprotein nitrogen than in my cases, but the actual values for urea nitrogen obtained by them were less.

Discussion.—It is therefore apparent that infants suffering from intestinal intoxication show a marked increase of nonprotein nitrogen and urea in the blood. The nonprotein nitrogen of the blood consists of urea, uric acid, creatin, creatinin, ammonia, amino-acids and probably other substances of unknown nature. As shown in Table 2, the increase in nonprotein nitrogen is due in part only to urea, which comprises less than 50 per cent. of the total nonprotein nitrogen. Determinations of the amounts of uric acid, creatinin, ammonia and amino-acids in this series of cases would have been of interest and perhaps of practical importance, but they were not made, as more blood would have been required than we felt justified in taking. Determinations of these substances, however, have been made in individual cases and are being concluded at the time of preparing this article.

In three cases of the present series uric acid and creatinin were determined and a decided increase found. The results were as follows:

Case	Nonprotein N. Mg. per 100 C.c. Blood	Urea N. Mg. per 100 C.c. Blood	Uric Acid. Mg. per 100 C.c. Blood	Creatinin. Mg. per 100 C.c. Blood
21	189.0	71.9	18	3.0
22	140.0	59.7	21	2.1
23	159.6	63.2	10	2.9

TABLE 2.—THE NONPROTEIN NITROGEN AND UREA NITROGEN IN THE BLOOD OF INFANTS WITH INTESTINAL INTOXICATION *

Number	Date	Age, Months	Weight		Carbon Dioxid Tension of Alveolar Air, Mm.	C.c. of CO_2, Reduced to 0, 760 Mm., Bound as Bicarbonate by 100 C.c. of Blood Plasma (Van Slyke)	Nonprotein Nitrogen, Mg. per 100 C.c. of Blood	Urea Nitrogen, Mg. per 100 C.c. of Blood
			Lb.	Oz.				
1	1/12	3	8	15	22.0	40.0†	140.0	62.3
	1/14‡				42.0	92.0	98.0	
	1/18				33.0		29.0	11.1
	1/24					65.0	28.0	
2	1/15	5	10		19.0	....	58.0	20.1
	1/16				20.0	36.0	123.0	
3	2/ 2	5½	12	4	14.7§	26.0	140.0	
	2/ 5				17.4§		193.2	
	2/ 6					34.0	184.8	
4	3/ 2	4	6	6	31.37§	....	137.0	
	3/ 3				21.0	42.0	193.0	
5	3/ 5	3	8	8	17.0	....	150.0	84.0
	3/ 6					38.0	169.0	75.6
6	3/10	5½	5	9	34.2§	....	83.0	39.0
	3/12					40.0	73.0	
	3/13				22.0		97.0	
7	3/19	4	13	6	35.1§	....	78.6	25.2
	3/20				17.2§			
	3/21					88.0		
	3/26‡				36.4§	100.0	57.0	15.9
8	4/18	9	17		28.4§	....	142.0	72.1
	4/19‡				56.0	97.0	127.0	64.3
	4/26					69.0	95.0	
9	.....	6	11	4	21.5§	40.0	84.0	39.7
10	.....	11½	12		17.0	....	61.9	
11	.....	13	15	3	23.4§	25.1	124.0	44.8
12	.....	6	12	8	25.0	....	133.0	39.1
13	5/16	5	11	12	23.0	....	134.4	
	5/17‡				37.5§	76.0	176.9	76.58
14	.....	8½	14	3	17.0	....	232.0	108.2
15	.....	5	10	4	23.6§	....	179.0	68.4
16	.....	7	13	1	26.1§	....	58.8	27.6
17	.....	8½	14	2	16.0	34.0	143.0	78.7
18	.....	9½	13	4	16.0	....	36.0	13.2
19	11/11	7	11	6	21.3§	....	176.0	89.0
	11/18‡				38.0		160.0	
	11/24						28.0	7.0
20	5/20	9	14	8	14.4§	23.2	211.0	96.1
	5/25‡				44.3§		50.1	13.4
21	5/23	9	14	4	24.6§	....	189.0	71.9
	5/27‡				39.6§		34.0	14.0
22	6/ 1	10	15	6	23.0	....	140.0	59.7
23	.....	13	19		25.0	....	159.6	63.2

* This table includes only part of the cases, as forty-four cases of intestinal intoxication were investigated. The results were so uniform that it seemed superfluous to tabulate all cases. Some of the additional cases will be cited in the text.

† These values are cited merely in general confirmation of the alveolar air analyses. They cannot be compared accurately with the figures for alveolar air, since the values for the carbon dioxid of alveolar air represent venous blood while the plasma analyses are probably more nearly representative of arterial blood. In a late series of cases, to be reported shortly, this discrepancy has been eliminated.

‡ After treatment. The treatment comprised the administration of 2 to 7 gm. of sodium bicarbonate by subcutaneous or intravenous injection and giving large amounts of water by mouth, or salt solution subcutaneously or intravenously.

§ Air collected by the method of Plesch-Higgins as adapted to infants by Howland and Marriott and analyzed in the Haldane apparatus. The remaining figures represent alveolar air collected in the same way but determined by the colorimetric method of Marriott.

TABLE 3.—THE CORPUSCULAR VOLUME AND TOTAL SOLIDS OF THE BLOOD; THE SPECIFIC GRAVITY AND TOTAL NITROGEN OF THE BLOOD SERUM OF NORMAL INFANTS *

Number	Total Solids of the Blood, per Cent.	Corpuscular Volume of the Blood, per Cent.	Specific Gravity of the Blood Serum	Total Nitrogen of the Blood Serum, Gm. per 100 C.c.	Ratio of Nonprotein Nitrogen of Blood to Total Nitrogen of the Blood Serum N.P.N. : T.N.
1	....	35.2	1.021	1.123	1 : 34
2	....	34.3	1.026	1.088	1 : 31
3	....	38.9	1.024	1.101	1 : 27
4	....	42.0	1.023	0.9876	1 : 29
5	....	38.0	1.021	1.043	1 : 30
6	....	32.5	1.020	1.181	1 : 32
7	....	35.5	1.022	1.198	1 : 31
8	....	34.0	1.020	1.11	1 : 31
9	....	33.0	1.025	1.02	1 : 27
10	....	29.0	1.024	0.983	1 : 25
11	....	34.0	1.025	1.13	1 : 32
12	....	31.0	1.023	0.987	1 : 28
13	18.6	45.0	1.022	1.061	1 : 27
14	17.9	39.0	1.020	1.113	1 : 40
15	....	32.0	1.021	0.997	1 : 33
16	17.5	33.0	1.022	1.043	1 : 28
17	17.1	29.8	1.024	1.121	1 : 41
18	....	32.0	1.026	1.069	1 : 40
19	17.7	36.0	1.020	1.00	1 : 29
20	....	37.0	1.026	0.983	1 : 32
21	....	33.0	1.025	1.18	1 : 31
22	18.4	38.0	1.020	1.108	1 : 46
23	17.3	31.0	1.024	1.16	1 : 50
24	18.2	39.0	1.023	0.977	1 : 30
25	17.2	32.9	1.021	1.111	1 : 40
26	....	34.0	1.020	1.023	1 : 41
27	....	32.0	1.021	1.101	1 : 29
28	17.4	34.0	1.022	1.097	1 : 32
29	....	35.0	1.023	1.114	1 : 36
30	18.5	39.8	1.025	1.01	1 : 36

* The figures in this table were obtained from the same infants as those in Table 1 and are numbered the same. To avoid needless repetition the age, weight, etc., are not given in the foregoing table as they are shown in Table 1.

The substances comprising the nonprotein nitrogen are normally excreted in the urine, and an accumulation in the blood usually signifies an impairment of renal function. While this interpretation is generally accepted, yet in connection with infantile diarrhea another possibility must be considered. The loss of water through the bowels in diarrhea is one of the most prominent clinical features of the disease and the question naturally arises whether this loss of water could be responsible for the high nonprotein nitrogen in the blood. If the blood became more concentrated through loss of water, it seems possible that there could be a relative increase of nonprotein nitrogen due to this cause. Such an increase, however, would be merely apparent.

To obtain evidence bearing on this possibility, determinations of the blood concentration were made.

II. THE CONCENTRATION OF THE BLOOD

1. *Corpuscular Volume.*—This was determined in the special pipet of Gettler and Baker[3] and in the manner described by them.

The corpuscular volume of normal infants ranges from 31 to 42 volumes per cent. (Table 3). Gettler and Baker found in normal adults that the corpuscular volume ranged from 33 to 50 volumes per cent., which values are considerably higher than those in normal infants.

In cases of intestinal intoxication the values were from 32 to 49 volumes per cent. (Table 4). Comparison of Tables 3 and 4 shows that in cases of intestinal intoxication the average corpuscular volume is higher, and in a number of the individual cases this increase is marked. The corpuscular volume, however, is not regularly increased in the cases of intoxication, and in a number of instances, despite the increase in nonprotein nitrogen, the corpuscular volume was within normal limits. Of most significance was the fact that there was no direct ratio between the corpuscular volume and the nonprotein nitrogen. For example, Case 5 showed a corpuscular volume of 38 and a nonprotein nitrogen of 150 mg. per 100 c.c. of blood, and later a corpuscular volume of 30 and a nonprotein nitrogen of 169. In both instances the corpuscular volume is within normal limits while the nonprotein nitrogen is greatly increased. Moreover, the second determination showed a lower corpuscular volume in the presence of a slightly increased nonprotein nitrogen. The same evidence is shown in several of the tabulated cases.

These determinations show that there is no constant decrease of the blood plasma in relation to corpuscles and that according to these results the high nonprotein nitrogen in cases of intestinal intoxication cannot be explained on the basis of increased blood concentration.

This argument would be valid only if, in intestinal intoxication, there was no increased destruction of red cells and if the red cells were

TABLE 4.—THE CORPUSCULAR VOLUME AND TOTAL SOLIDS OF THE BLOOD; THE SPECIFIC GRAVITY AND TOTAL NITROGEN OF THE BLOOD SERUM OF INFANTS WITH INTESTINAL INTOXICATION *

Number	Date	Total Solids of the Blood, per Cent.	Corpuscular Volume of the Blood, per Cent.	Specific Gravity of the Blood Serum	Total Nitrogen of the Blood Serum, Gm. per 100 C.c.	Ratio of the Nonprotein Nitrogen of the Blood to the Total Nitrogen of the Blood Serum N.P.N : T.N.
1	1/12	....	36.0	1.0279	1.297	1 : 10
	1/14		37.0	1.025	1.36	1 : 14
	1/18		32.0	1.022	1.11	1 : 38†
2	1/15	....	39.5	1.026	—	
	1/16	21.8	—	1.027	1.55	1 : 13
3	2/ 2	....	47.0	1.029	1.36	1 : 10
	2/ 6	20.4	34.0	1.029	1.219	1 : 6
4	3/ 2	....	32.0	—	—	
	3/ 3	20.9	31.0	1.030	1.368	1 : 7
5	3/ 5	20.6	38.0	1.031	—	
	3/ 6	19.7	30.0	1.027	1.112	1 : 7
6	3/10	21.1	—	1.026	1.114	1 : 13
	3/12	20.0	—	—	0.914	1 : 12
	3/13		37.0	1.030	1.28	1 : 13
7	3/19	....	49.0	1.030	1.176	1 : 15
	3/21		39.0	—	—	
	3/26	20.8	35.0	1.024	0.985	1 : 17
8	4/18	21.6	37.0	1.032	1.513	1 : 11
	4/19	21.1	42.0	1.030	1.42	1 : 11
	4/26	19.3	27.0	1.026	0.942	1 : 10
9	....	....	—	—	—	
10	....	....	35.0	1.024	1.057	1 : 17
11	....	....	39.0	1.030	—	
12	....	20.8	49.0	1.028	1.218	1 : 9
13	5/16	21.3	42.0	1.029	1.358	1 : 10
	5/17		37.0	1.026	1.204	1 : 7
14	....	?1.1	49.0	.....	1.36	1 : 6
15	....	....	....	1.030	1.302	1 : 7
16	....	17.4	....	1.023	0.980	1 : 17
17	....	....	47.0	1.029		
18	....	....	29.0	1.026		
19	11/11	19.9	39.6	1.030	1.3	1 : 7
	11/18		38.4		1.23	1 : 8
	11/24	18.9†	34.0	1.027	1.09	1 : 39†
20	5/20	21.7	39.8	1.031	1.365	1 : 6
	5/25	19.1†	37.0	1.025	1.071	1 : 22†
21	5/23	21.6	45.0	1.029	1.361	1 : 7
	5/27	18.5†	38.9	1.023	1.14	1 : 33†
22	....	....	49.9	1.030	1.298	1 : 9
23	....	....	46.2	1.031	1.321	1 : 8

* The figures in this table were obtained from the same infants as those in Table 2 and are numbered the same. To avoid needless repetition the age, weight, etc., are not given in the above table as they are in Table 2. See footnotes * and ‡ Table 2.

† After treatment.

of normal size. Obviously, a marked destruction of red cells would decrease the corpuscular volume while an increase or decrease in the size of the cells would be of marked influence. Whether there is an increased blood destruction in intestinal intoxication is impossible to say, but there is no evidence to support such a view. Fresh blood preparations have been examined in a number of cases and these showed no apparent change in the size of the red cells.

2. *Specific Gravity of the Blood Serum.*—The specific gravity was determined by weighing the blood serum in small Nicholl pyknometers with a capacity of from 0.4 to 1.5 gm. of water. All determinations were at 22 C.

The specific gravity of the blood serum of normal infants varies from 1.020 to 1.025 (Table 3). These values are lower than those in normal adults, which, according to Gettler and Baker,[3] are from 1.026 to 1.030. In cases of intoxication the specific gravity was from 1.026 to 1.031, which is greater than that of normal infants. This increase, however, is too slight to account for the increase in nonprotein nitrogen merely on the basis of increased blood concentration.

Assuming that the normal specific gravity of the blood serum of infants is 1.020, this signifies that each 100 c.c. of blood serum contains 2 gm. of dissolved solids. An increase of the specific gravity to 1.031, which was the maximum found in cases of intoxication, would indicate an increase of 1.1 gm. of solids per 100 c.c. This would merely signify that the serum contained a trifle more than one and one-half times as much solids as normal. In the cases of intestinal intoxication, we find that the nonprotein nitrogen is often five times as great as normal, and if this increase were merely a matter of increased blood concentration, all solids should be equally affected and the specific gravity should be as great as 1.100. In no instance was the specific gravity increased to any degree comparable to the increase in nonprotein nitrogen. Moreover, a comparison of the nonprotein nitrogen and specific gravity in cases of intoxication shows that there is no direct ratio and that in several instances there was a great increase in the nonprotein nitrogen, with a specific gravity within the limits of normal. Moreover, the mere increase in nonprotein nitrogen would cause an increase in the specific gravity of the serum aside from any increase in concentration due to loss of fluid from the blood.

3. *Total Nitrogen of the Blood Serum.*—One half to 1 c.c. of blood serum was digested in a small Kjeldahl flask with 2 c.c. of sulphuric acid, about 0.5 gm. of potassium sulphate and a small crystal of copper sulphate. The determination was made by aeration into twentieth-normal acid and titration with twentieth-normal sodium hydroxid, using congo red as indicator.

If the increase of nonprotein nitrogen in the blood of infants suffering from intestinal intoxication is due merely to increased concentra-

tion of the blood, there should be a similar increase in the other substances comprising the total nitrogen of the blood. That such is not the case is readily seen by referring to Tables 3 and 4.[6] While there is a greater total nitrogen of the blood serum in cases of intoxication, this increase is in no way comparable to the increase of nonprotein nitrogen, and in several cases the increase in total nitrogen can be explained almost entirely by the increase in nonprotein nitrogen. This is shown best by comparing the nonprotein nitrogen: total nitrogen ratio in the normal cases with those of intoxication.

4. *Total Solids of the Blood.*—The total solids were determined by weighing a few drops of blood on blotting paper previously weighed, drying at 110 C. and again weighing.

As shown in Table 3, the total solids in normal infants ranged from 17.1 to 18.6 per cent. In cases of intoxication (Table 4) the values were from 19.6 to 21.8 per cent. These figures agree closely with those recently published by Courtney and Fales[7] and have the same significance as those for corpuscular volume, total nitrogen and specific gravity.

TABLE 5.—SHOWING THE RETENTION OF NONPROTEIN NITROGEN AND UREA AFTER THE BLOOD CONCENTRATION BECAME NORMAL

Date	Weight, Pounds	Nonprotein Nitrogen, Mg. per 100 C.c. of Blood	Urea Nitrogen, Mg. per 100 C.c. of Blood	Specific Gravity of Blood Serum	Total Nitrogen in Blood Serum, Gm. per 100 C.c.	Corpuscular Volume, per Cent.
11/11	11⅝	176	89	1.030	1.301	39.6
11/18	11	160	..	.....	1.23	38.4
11/20	11⅝	120	50	1.026	1.18	34.5
11/22	11¾	100	..	1.025	1.12	
11/24	11⅞	28	7	1.024	1.09	34.0

Baby G. (Case 19) was admitted Nov. 11, 1916, with a history of severe diarrhea and vomiting for four days. The infant was greatly emaciated and the fontanel was sunken. The mental condition was dull. Hyperpnea was marked and the carbon dioxid tension of the alveolar air was 19 mm.

Seven and a half grams of sodium bicarbonate were given by intravenous injection. The carbon dioxid tension of the alveolar air became normal and the hyperpnea ceased. Large amounts of water were given by mouth and by subcutaneous injection (physiologic sodium chlorid solution).

Discussion.—It is of interest that the corpuscular volume of the blood, the total solids of the blood, the total nitrogen and specific gravity of the blood serum are all much lower in normal infants than in

6. In adults Gettler and Baker (Footnote 3) found that the total nitrogen of the blood serum was from 1.2 to 1.4 gm. per 100 c.c. These values are much greater than those from normal infants.

7. Courtney, A. M., and Fales, H. L.: AM. JOUR. DIS. CHILD., 1917, **14**, 202.

adults. This is probably in correspondence with the fact that the tissues of the infant contain a higher percentage of water and that the water metabolism is more active in infants than in adults.

The data furnished by the total nitrogen, specific gravity, corpuscular volume and total solids indicate that in intestinal intoxication there is often an increase in blood concentration. This increase in concentration, however, is insufficient to account for the increase in nonprotein nitrogen found in these cases.

Further evidence bearing on this question is the observation that a number of patients begin to retain fluid for some time before the nonprotein nitrogen falls to normal. The nonprotein nitrogen remains high after the corpuscular volume of the blood and total nitrogen and specific gravity of the serum reach normal. This would indicate that the high nonprotein nitrogen was not due merely to the increased blood concentration. The results from a case of this kind are shown in Table 5.

On the basis of the evidence given it seems that the increased nonprotein nitrogen which occurs in cases of intestinal intoxication is due to defective elimination of the nitrogenous waste products by the kidney.

III. TESTS OF RENAL FUNCTION. PHENOLSULPHONEPHTHALEIN ELIMINATION: AMBARD'S COEFFICIENT OF UREA EXCRETION

Phenolsulphonephthalein Elimination: Technic.—The infant was put on a metabolism frame three hours after the last feeding and was given 120 c.c. of slightly sweetened water. Three mg. of phenolsulphonephthalein were given intramuscularly and the urine collected for two hours. One half of the urine was used to determine the phthalein in a Rowntree and Geraghty modification of the Autenreith-Königsberger colorimeter; the other half was used for estimation of urea, ammonia and total nitrogen.

Tests were made on thirty normal infants from 3 months to 1 year of age. The phenolsulphonephthalein elimination ranged from 58 to 94 per cent. during two hours, the water elimination from 56 to 100 c.c. (47.5 to 83.5 per cent.). (Table 6.)

The results from 16 infants with intoxication are shown in Table 7. The phenolsulphonephthalein elimination was from 4 to 38 per cent., the water elimination from 23 to 48 c.c. (19 to 40 per cent.). The interpretation of these results in terms of renal permeability cannot be made with any degree of assurance, owing to the greatly diminished secretion of urine. During the acute stage of intestinal intoxication the infant may pass no urine for hours and the twenty-four hour elimination may total only a few cubic centimeters. For this reason, in the cases of intestinal intoxication used for the phenolsulphonephthalein test the patients had recovered from the acute stage and had commenced

TABLE 6.—THE ELIMINATION OF WATER AND PHENOLSULPHONEPHTHALEIN; AMBARD'S COEFFICIENT OF UREA EXCRETION. NORMAL INFANTS

Number	Age, Months	Weight, Pounds	Water Elimination after Ingestion of 120 C.c. of Water, 2 Hour Period		Phenol-sulphone-phthalein Output, 2 Hour Period, per Cent.	Ambard's Coefficient of Urea Excretion, 2 Hour Period, Ur $\checkmark D\frac{\sqrt{c}}{\sqrt{5}}$
			C.c.	per Cent.		
1	3	11¼	66	55.0	80	0.072
2	3½	10⅝	80	67.5	64	0.061
3	4	12½	90	75.0	68	0.096
4	4	11¾	58	47.5	96	0.084
5	5	13	74	61.5	58	0.10
6	5½	13½	94	78.0	73	0.071
7	6	14½	59	49.0	67	0.05
8	6	15	67	56.0	74	0.11
9	6½	14¾	86	71.5	88	0.065
10	7	16½	73	61.0	71	0.098
11	7	16	81	62.5	81	0.061
12	7½	15½	59	49.0	61	0.01
13	8	16¾	62	52.0	70	0.072
14	8	17½	56	47.5	59	0.076
15	10½	18	79	66.0	86	0.068
16	11	19½	100	83.5	94	0.05
17	12	20¾	77	64.0	87	0.078
18	13	21	67	56.0	75	0.087
19	13	20½	99	82.5	71	0.061
20	13½	21¼	78	65.0	78	0.072

to pass moderate amounts of urine. No test was included during which less than 20 c.c. of urine was voided. Despite the selection of cases and the fact that 120 c.c. of water were ingested at the time of the test, the water output was greatly diminished. As shown by Tables 6 and 7, the phenolsulphonephthalein elimination was greatly diminished in cases of intoxication. Owing to the decreased secretion of urine the low phenolsulphonephthalein output cannot be attributed to an anatomic kidney lesion.

Ambard's Cofficient of Urea Excretion.—According to Ambard[8]

8. Ambard, L.: Physiologie normale et pathologique des reins, Paris, 1914; Ambard, L., and Weill, A.: Jour. de physiol. et de pathol. gén., 1912, **32,** 217. This subject has also been considered in detail by McLean, F. C., and Selling, L.: Jour. Biol. Chem., 1914, **19,** 31; McLean, F. C.: Jour. Exper. Med., 1915, **22,** 212; Addis, T., and Watanabe, C. K.: Jour. Biol. Chem., 1916, **24,** 203, and Lewis, D. S.: Arch. Int. Med., 1917, **19,** 1.

TABLE 7.—The Elimination of Water and Phenolsulphonephthalein; Ambard's Coefficient of Urea Excretion. Infants with Intestinal Intoxication *

Number	Age, Months	Weight, Pounds	Water Elimination after Ingestion of 120 C.c. of Water, 2 Hour Period		Phenol-sulphone-phthalein Output, 2 Hour Period, per Cent.	Ambard's Coefficient of Urea Excretion, 2 Hour Period, $\frac{Ur}{\sqrt{D\frac{\sqrt{c}}{\sqrt{5}}}}$
			C.c.	per Cent.		
1	3	8¾	26	13.0	22.0	0.23
2	4½	9¼	31	26.0	18.0	0.31
3	5	9	40	33.0	29.0	0.21
4	5¾	10	25	31.0	34.0	0.19
5	6¼	9¾	48	40.0	34.0	0.22
6	7½	12¼	35	29.0	17.0	0.36
7	7¾	11¾	29	24.0	20.0	0.27
8	8	13½	31	26.0	23.0	0.29
9	8½	12¾	23	19.0	15.5	0.27
10	9	14	47	40.0	38.0	0.10
11	9	13½	36	30.0	27.0	0.17
12	10½	12¾	28	23.0	14.0	0.37
13	10¾	13¼	30	25.0	30.0	0.20
14	11	14	37	31.0	29.0	0.27
15	11½	12⅞	44	37.0	39.0	0.18
16	11¾	15½	33	27.5	20.0	0.:3

* During the acute stage of intestinal intoxication so little urine is secreted that tests of renal function are impossible. The figures shown were derived from a study of patients who had begun to improve and who excreted more than 20 c.c. of urine during the two-hour period.

and his co-workers there is a definite ratio between the urea in the circulating blood and that excreted in the urine per unit of time. The formula used to derive the coefficient is obtained from Ambard's third law and is as follows:

$$K = \frac{Ur}{\sqrt{D\frac{70}{P}\frac{\sqrt{C}}{\sqrt{25}}}}$$

K=Coefficient of urea excretion.

Ur=Urea per liter of blood.

D=Output of urea for twenty-four hours calculated from the amount excreted during the period of observation.

P=Weight of patient in kilograms.

C=Grams of urea per liter of urine.

70=Standard weight.

25=Normal amount of urea per liter of urine.

Our observations were made during two-hour periods at the same time the phenolsulphonephthalein tests were made. The analytical methods were those previously described.

In applying Ambard's formula to infants it is obvious that certain changes must be made. In the formula the standard weight of 70 kg. is used. This is, of course, relative to adults. It is practically impossible to introduce a standard weight for young infants owing to the fact that the weight changes are so rapid. The use of the average weights for different ages would not be strictly accurate, since the weights of normal infants of the same ages may vary within several pounds, which makes a considerable error when one considers such differences in relation to total weight. A further difficulty arises from the circumstance that infants with nutritional disorders show great fluctuations in weight within short periods of time. Actual calculations in normal cases show that the coefficient is more constant if the factor 70/P or any equivalent is eliminated.

For adults the standard value of 25 gm. of urea per liter of urine is used. Our determinations on thirty normal infants under 1 year of age gave figures which ranged from 4.2 to 6.37 gm. of urea per liter. On the basis of these figures the standard value of 5 was substituted for 25 in the formula. As used by us the formula was as follows:

$$K = \frac{Ur}{\sqrt{D\frac{\sqrt{C}}{\sqrt{5}}}}$$

In adults it has been found that the normal coefficient ranges from 0.6 to 0.9 and that defective kidney function causes the constant to increase. In normal infants the constant, as calculated by the formula we used, ranges from 0.05 to 0.11 (Table 6). The coefficient, therefore, has a tendency to be higher in infants than in adults, and in several of our normal cases values above 0.09 were obtained which in adults would signify impairment of renal function.

In cases of intoxication the constant ranged from 0.13 to 0.39, thus indicating a considerable degree of impairment of renal function (Table 7).

In general, these results are roughly parallel to the phenolsulphonephthalein elimination and are open to the same criticism in reference to the excretion of water. All that these tests signify is that in intestinal intoxication the power of elimination by the urine is greatly impaired.

IV. THE CAUSE OF DEFICIENT ELIMINATION BY THE KIDNEYS

In consideration of the greatly diminished excretion of urine during the acute stage of intestinal intoxication it seems only natural to expect that substances normally excreted in the urine would be retained. This would certainly occur unless there were some other channel through which the waste products could be eliminated. Despite the self evidence of this proposition it is a question of some importance whether the retention is entirely a matter of lessened water excretion, or whether it is dependent on a kidney lesion.

The occurrence of albumin and casts in the urine of infants affected with severe diarrhea has long been recognized and is mentioned in practically every treatise on this disease. The subject was considered in detail by Pick,[9] in 1905, who gave an exhaustive review of the literature. He noted that the toxic symptoms in severe diarrhea are not unlike those of uremia, and suggested the possibility that in some cases the symptoms may be of uremic origin.

Neuman,[10] in 1907, found that in general there was a close parallel between the presence and degree of albuminuria and cylindruria and the severity of the toxic symptoms. He concluded, however, that the renal lesions were probably secondary and not of etiologic importance.

In all of the cases in this series the urine contained albumin and casts during the acute stage of the disease. With improvement in the symptoms, albumin and casts soon disappeared. The degree of albuminuria, however, was rarely great and not often of sufficient amount to give a reading in the Esbach tube. In most instances the number of casts seemed much greater than one would expect from the amount of albumin present. The period at which the albuminuria and cylindruria were most marked coincided with the period when the urine was very scanty, so that the number of casts, at least, would appear much greater than it actually was.

A detailed consideration of the significance of albumin and casts in the urine is beyond the scope of this paper. Certainly their presence is abnormal, but whether their occurrence indicates a kidney lesion capable of causing retention of nitrogenous waste products is impossible to determine. It does seem clearly established, however, that the occurrence of albuminuria and cylindruria does not necessarily indicate a kidney lesion which is demonstrable by our present histologic methods. If definite anatomic lesions are the sole criteria of kidney disease, we should not be warranted in assuming that a kidney lesion was present solely on the basis of albuminuria and cylindruria.

9. Pick, J.: Arch. f. Kinderh., 1905, **40**, 291.
10. Neuman, G.: Jahrb. f. Kinderh., 1907, **66**, 633.

Neuman[10] found slight parenchymatous renal lesions in one of his cases. In another, the kidneys were practically normal. Pick,[9] however, found distinct anatomic lesions in several cases. Definite renal lesions in infants dying of intestinal intoxication were described by Hoffsten,[11] Epstein,[12] Bernhard and Felsenthal,[13] Czerny and Moser,[14] Jehle[15] and others.

In nine of the cases presented in this paper necropsies were performed and the results are shown in Table 8. In two cases, 14 and H., there was distinct parenchymatous nephritis, severe in one (14) and moderate in the other (H.). In both of these cases the tubules contained many necrotic cells which were often massed to form distinct foci. These foci stained a deep blue with hematoxylin, which suggested the deposition of calcium salts. The lesions in these cases resembled closely those seen in poisoning with mercuric chlorid. Three cases, 10, 5 and O'D., showed no definite renal changes at all. The remaining four cases showed slight or moderate parenchymatous changes in the tubular epithelium and hemorrhage into the tubules. Dr. Charles Norris, who kindly examined the sections, stated that the hemorrhage was possibly agonal and in consequence may have borne no direct relation to the disease. This is suggested strongly by the fact that the urine of none of these patients contained blood, which should have been true had the hemorrhage existed for some time before death.

Unfortunately, there is no evidence available which indicates the degree of kidney damage necessary to cause retention. On the basis, however, of the lesions present in nephritis in adults with nonprotein nitrogen retention it would seem that in only two of our cases was the kidney lesion sufficient to account for the high nonprotein nitrogen. Lesions of similar grade to those found in the other cases are often found in the absence of any chemical evidence of defective renal function.

It seems apparent, therefore, that the impairment of renal function in intestinal intoxication cannot be due in the majority of cases to a definite kidney lesion, but must depend on some other cause. It seems most probable that the cause lies in the depleted water supply of the body.

It is well established that water is the most efficient diuretic, and without an adequate supply secretion of urine is impossible. In intestinal intoxication the water supply of the body is usually depleted by the great loss of water in the stools. Many of the patients refuse to

11. Hoffsten: Virchow-Hirsch Jahresb., 1888, **11,** 478.
12. Epstein: Festschrift Edw. Henoch, Berlin, 1890.
13. Bernhard and Felsenthal: Arch. f. Kinderh., 1894, **17,** 222.
14. Czerny and Moser: Jahrb. f. Kinderh., 1894, **38,** 430.
15. Jehle: Jahrb. f. Kinderh., 1907, **65,** 40, Part 1.

TABLE 8.—Evidences of Renal Involvement in Nine Cases of Intestinal Intoxication

Patient	Nonprotein Nitrogen, Mg. per 100 C.c. of Blood	Albumin in Urine	Casts in Urine	Evidence of Renal Lesions	
				Macroscopic	Microscopic
10*	61.9	+ Trace	Few hyaline many granular	Moderate congestion; no swelling of cortex; markings distinct	No significant lesions
13*	134.4	Heavy trace	Many hyaline granular and epithelial	Cortex pale, slightly swollen; markings slightly obscured	Many tubules contain red blood cells; tubular epithelium shows parenchymatous degeneration; apparent increase in nuclei in malpighian corpuscles, possibly due to shrinkage
14*	232.0	1 Gm. per liter by Esbach	Many granular and epithelial†	Kidneys pale; greatly enlarged; edematous; cortex much swollen and markings obscured	Marked swelling and necrosis of tubular epithelium; foci of necrotic cells in tubules of cortex; coagulated material in glomeruli; apparent increase in number of cells in malpighian tufts; definite acute parenchymatous nephritis
6*	83.0	Trace	Many hyaline few granular	Kidneys slightly enlarged; cortex slightly swollen	Moderate swelling and parenchymatous degeneration of tubular epithelium; nuclei slightly pale
5*	150.0	Trace	Many hyaline few granular	Slight congestion	No significant lesions
P	113.4	Trace	Few hyaline many granular	Kidneys pale; slightly enlarged; cortex slightly swollen; slight edema	Many tubules contain red blood cells; parenchymatous degeneration of tubular epithelium
H	65.8	Moderate 1.5 Gm. per liter by Esbach	Many hyaline and granular	Kidneys pale; slight swelling of cortex	Marked hemorrhage into tubules of pyramids; hemorrhage into glomeruli; necrosis of tubular epithelium with the formation of a few necrotic foci in tubules; acute parenchymatous nephritis
V	90.3	Trace	Many hyaline few granular	Slight enlargement of kidneys; marked congestion	Hemorrhage into tubules; tubular epithelium shows moderate parenchymatous degeneration
O'D	68.0	Trace	Many hyaline few granular	Slight congestion	No significant lesions

* These figures refer to the same patients as those in Tables 2 and 4.
† A few red blood cells in urine.

ingest even water and vomit water or food, so that there is but little fluid available to replace even the normal loss of water in the excretions. It seems probable, therefore, that the deficient elimination by the kidney is purely functional and is due to the fact that there is no water available for the formation of urine.

The fact that the increased concentration of the blood is insufficient to account for the high nonprotein nitrogen is in no way antagonistic to this idea. There are a number of factors which tend to keep normal the water composition of the blood.

Bang[16] found that when dogs are deprived of water the blood shows increased nonprotein nitrogen. The nonprotein nitrogen became normal when water was given in sufficient amounts. Bang gave no evidence bearing on the blood concentration. It seems quite possible that the high nonprotein nitrogen was due to defective elimination owing to lack of water.

The clinical importance of the great loss of water in intestinal intoxication is too well known to require special consideration. It is a matter of considerable difficulty to give these infants sufficient water to replace that lost in the excretions. In six cases of intoxication in which it was possible to give sufficient water approximately to replace that lost the excretion of urine was apparently normal and there was no significant increase in the nonprotein nitrogen of the blood. Of the same significance is the fact that in no case was there any material reduction in the nonprotein nitrogen of the blood before the normal excretion of urine was restablished.

From the evidence at our disposal it seems probable that the deficient kidney elimination in intestinal intoxication is dependent, to a great degree at least, on the negative water balance. Whether insufficient water in the blood and tissues is directly and entirely responsible for the diminished secretion of urine offers considerable field for discussion. There are a number of factors capable of affecting kidney function which may be of influence. It has been demonstrated by Starling[17] that the colloids of normal blood exert an osmotic pressure of 25 to 30 mm. of mercury and under these conditions the arterial pressure in the kidney glomeruli must be greater than 30 mm. of mercury to insure the formation of urine. A greater concentration of colloids would require a greater arterial pressure in the kidney for glomerular filtration to occur.

In intestinal intoxication it seems possible that the blood colloids may be increased to such degree that they exert an osmotic pressure greater than the pressure in the glomerular capillaries. If this were

16. Bang, I.: Biochem. Ztschr., 1915, **72,** 119.
17. Starling: Jour. Physiol., 1899, **24,** 317.

true the formation of urine would be prevented. Moreover, the total blood volume is probably reduced in cases of intestinal intoxication, which would diminish the blood flow through the kidney and consequently reduce the secretion of urine. Such conditions, however, would arise in great part, if not entirely, from the water deficit and at present have not been accurately determined.[18]

V. THE ACIDOSIS OF INTESTINAL INTOXICATION

Howland and Marriott[19] showed that acidosis is a frequent occurrence in severe diarrhea in infants. The frequency and degree of acidosis in cases of intestinal intoxication has been discussed also by Schloss and Stetson.[20]

According to our present conception, acidosis is best defined as a reduction in the alkaline reserve of the blood. Our knowledge of the significance of the alkaline reserve and the factors which influence it is based on the work of Henderson[21] and Henderson and Palmer,[22] and has been discussed by Lundsgaard,[23] Peabody.[24] Hasselbalch and Gammeltoft,[25] Barcroft,[26] Howland and Marriott,[27] Van Slyke and Cullen[28] and others.

On the basis of this definition it is theoretically possible for acidosis to be due to several causes. In acidosis occurring with diarrhea Howland and Marriott[19] found no evidence that abnormal acids were formed. They found no significant increase in the acetone bodies in the blood, which demonstrated that the acidosis was not due to increased formation or diminished oxidation of these substances.

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18. There is no means of ascertaining the blood pressure in the kidney of human beings. In dogs it is assumed to be 20 per cent. less than the carotid blood pressure, but Cushny states that such assumption is little more than a guess (The Secretion of Urine, London, 1917). MacKenzie (Brit. Jour. Child. Dis., 1912, **9,** 343) says that the anuria in severe diarrhea of infants is due to lowered blood pressure, although he gives no evidence to support this view. Hill (Arch. Pediat., 1913, **30,** 588) has reported blood pressure determinations (femoral artery) in eighteen cases of severe diarrhea. His results show no reduction in blood pressure when compared with the values for normal infants obtained by Morse and Wyman (Am. Jour. Dis. Child., 1914, **8,** 270) and others.

19. Howland, J., and Marriott, W. McK.: Am. Jour. Dis. Child., 1916, **11,** 309.

20. Schloss, O. M., and Stetson, R. E.: Am. Jour. Dis. Child., 1917, **13,** 218.

21. Henderson, L. J.: Am. Jour. Physiol., 1908, **21,** 427; Ergebn. d. Physiol., 1909, **8,** 254; Jour. Biol. Chem., 1911, **9,** 403.

22. Henderson, L. J., and Palmer, W. W.: Jour. Biol. Chem., 1912-1913, **8,** 393; 1913, **14,** 81; 1914, **17,** 305.

23. Lundsgaard, C.: Biochem. Ztschr., 1912, **41,** 149.

24. Peabody, F. W.: Arch. Int. Med., 1914, **14,** 236.

25. Hasselbalch, K. A., and Gammeltoft, S. A.: Biochem. Ztschr., 1915, p. 205.

26. Barcroft, J.: The Respiratory Function of the Blood, Cambridge, 1914.

27. Howland, J., and Marriott, W. McK.: Bull. Johns Hopkins Hosp., 1916, **27,** 63.

28. Van Slyke, D. D., and Cullen, G. E.: Jour. Biol. Chem., 1917, **30,** 289.

There is no evidence that the acidosis is caused by abnormal loss of alkali, for, as pointed out by Howland and Marriott, the analyses of diarrheal stools by Holt, Courtney and Fales show actually a loss of more acid than base. Nor can there be any signficant loss of alkali in the urine, for both the hydrogen-ion concentration and the titrable acidity are increased.

Howland and Marriott concluded that the acidosis of diarrhea was probably dependent on defective elimination of acid by the kidney and suggested the possibility that it was due, in part, at least, to the failure of the kidney to eliminate acid sodium phosphate. Recently, they have found that there is a considerable increase in the inorganic phosphorus in the blood, which is in accord with this view.[29]

The evidence derived from my own cases is entirely in accord with the view that the acidosis of intestinal intoxication is due to faulty elimination by the kidney. The blood has been examined for acetone bodies in six cases with severe acidosis, and in no case was the amount greater than could be accounted for by starvation. The greatest value was 37 mg. of total acetone bodies, determined as acetone, in 100 c.c. of blood.

In a great number of cases of relatively severe acidosis in intestinal intoxication, a single dose of sodium bicarbonate is sufficient permanently to correct the acidosis. It would seem most unlikely that this could occur if abnormal acids were being formed in large amounts. As an example the following protocol is given:

Protocol 1.—The patient, a boy, aged 6 months, was admitted Jan. 15, 1916. For two days before admission he had vomited almost every feeding and had many loose yellow stools. For twelve hours he had marked muscular twitchings, was semistuporous and refused all food. On admission the infant was somnolent, had distinct hyperpnea and seemed very ill.

Date	Carbon Dioxid Tension, Alveolar Air, Mm.	C.c. of CO_2, Reduced to 0, 760 Mm., Bound as Bicarbonate by 100 C.c. of Blood Plasma (Van Slyke)
1/15	22	34.6
	3 gm. sodium bicarbonate by intravenous injection	
1/16	40	80.0
1/18	39	72.0
1/20	41	69.0
1/25	37	68.0

The hyperpnea disappeared entirely after the bicarbonate and the stupor lessened but did not disappear. The diarrhea continued until January 20, and during this period the infant was toxic and very ill. Improvement began January 20 and January 25 the infant was practically free from symptoms. A single dose of alkali was therefore sufficient to eliminate entirely a marked degree of acidosis.

29. Personal communication, Dr, John Howland, Dec. 11, 1917.

It might be suggested that in cases of this type the acid formation had perhaps occurred at a time before the patient came under observation and had ceased, so that the single dose of alkali was sufficient, merely because no acid formation was in progress at that time. Such objection, however, would be invalid in the cases in which the acidosis developed under observation. Five cases of this type have been studied, an example of which is given in illustration:

Protocol 2.—Case 22, boy, aged 10 months. The baby had from eight to ten loose stools daily for five days; the day before admission he refused all food and became somnolent. On admission he showed evidence of moderate fluid loss and his expression was dull. There was no hyperpnea. The development of acidosis is shown by the following data. On November 19 hyperpnea was noted.

Date	Carbon Dioxid Tension, Alveolar Air, Mm.	C.c. of CO_2, Reduced to 0, 760 Mm., Bound as Bicarbonate by 100 C.c. of Blood Plasma (Van Slyke)
11/14/16	36.0	64.0
11/16	36.0	65.1
11/17	30.0	....
11/18	27.0	....
11/19	23.0	38.0
	3.7 gm. sodium bicarbonate by intravenous injection	
11/20	40.0	87.0
11/21	42.0	....
11/23	37.5	....
11/25	37.5	80.0
Death		

In this case the acidosis developed under observation and was corrected by the administration of sodium bicarbonate. The hyperpnea disappeared; the other evidences of intoxication were influenced but little, and the infant died without further evidence of acidosis.

These observations are entirely in accord with the view that the acidosis is due to the failure of the kidney properly to fulfil its function of preserving the alkali reserve of the blood and contrary to its dependence on the formation of abnormal acids.

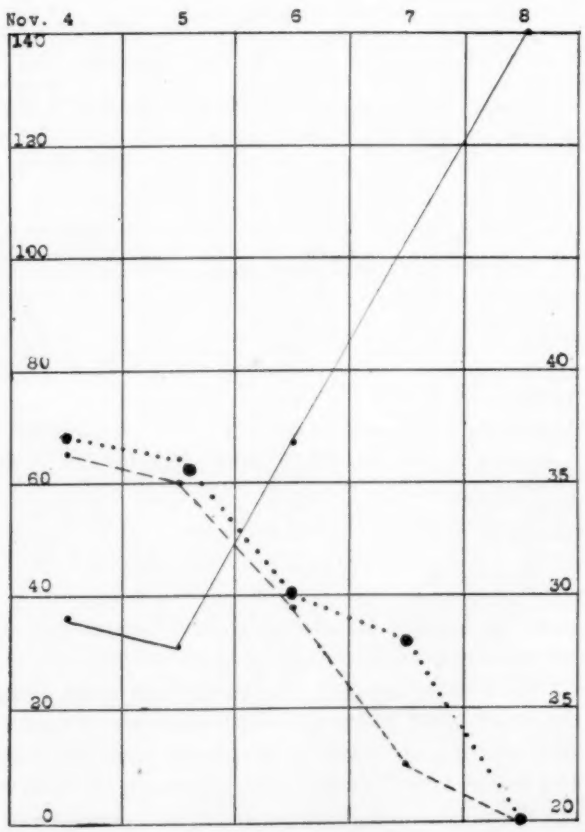
Evidence has been given which demonstrates that there is an accumulation of waste products in the blood due to defective secretion of urine. It seems only reasonable to suppose that the acidosis is of similar origin.

Six patients with intestinal intoxication have been observed to whom it was possible to supply approximately as much water as was lost. None of these patients showed a marked diminution in the excretion of urine and none developed acidosis.

In five cases the acidosis developed under observation. In three the output of urine was carefully observed, and in each instance the

acidosis was preceded by a diminished excretion of urine and the chemical evidence of impaired renal function. This occurrence is illustrated by the accompanying curve.

It would seem, therefore, that the acidosis of intestinal intoxication is probably due to defective kidney function.



Baby Y., aged 9 months. For three days previous to admission he appeared ill and passed from three to four loose green stools a day. During this period he vomited four times. On admission he was fairly nourished, the fontanel was not depressed and the skin was fairly moist and elastic. The infant was somnolent but could be roused easily. Until November 7 the food consisted of 3 ounces each of protein milk and barley gruel, given every four hours. In addition, large amounts of water were given. The stools were watery and from five to seven were passed in twenty-four hours. Vomiting became severe on November 8 and the food was changed to barley gruel. In the chart ----- with the figures at the left = urine in c.c. during a two-hour period after ingestion of 120 c.c. of water; ———— = nonprotein nitrogen of the blood in milligrams per 100 c.c.; ..... with the figures at the left = carbon dioxid tension, in millimeters, of the alveolar air.

VI. THE SYMPTOMS OF INTESTINAL INTOXICATION

To determine definitely at present the origin of the symptoms of intestinal intoxication is obviously impossible, but there are facts bearing on this question which seem of sufficient importance to mention.

In a number of cases the acidosis bears a definite relation to the symptoms. This is quite evident when the symptoms disappear promptly after the correction of the acidosis by alkali. In some of the cases there is but little improvement in the symptoms after acidosis is eliminated. Hyperpnea, if present, always disappears, but at times the patient remains semistuperous and the prostration and other manifestations remain unchanged. Although in such cases the symptoms cannot be due directly to acidosis, yet it seems possible that the lack of alkaline reserve had caused injury to the tissue which is not repaired by the mere correction of the existing acidosis. Even granting the correctness of this assumption, there are cases of intestinal intoxication in which the symptoms are marked and yet acidosis is absent. The symptoms in these cases, except that hyperpnea is absent, seem identical with those of cases in which acidosis is present. This is also true of those cases in which the symptoms improve after the administration of alkali but return within a short time despite the fact that there is no recurrence of acidosis.

The improvement which occurs after the administration of sodium bicarbonate is probably not always due entirely to the alkali. Part is due to the water, and moreover, in the regular treatment of these cases, large amounts of water are given independently of alkali.

While there seems no question that acidosis is an important cause of the symptoms of intestinal intoxication, yet it is by no means the whole cause.

There is no evidence to indicate that the retained nitrogenous waste products are responsible for the symptoms. It is generally believed that in uremia, even with considerable nonprotein nitrogen retention, these substances are not responsible for the toxic symptoms. Recently, Hewlett, Gilbert and Wickett[30] were able to cause toxic symptoms in normal adults by feeding large amounts of urea. The symptoms, however, were slight in comparison to the degree of urea retention in the blood and as compared with what is often observed in uremia. These experiments show that large amounts of retained urea can be toxic, yet they do not demonstrate that the amount of urea retained in intestinal intoxication can be the cause of the toxemia.

There is a close analogy between intestinal intoxication and uremia. Indeed, all of the evidence points directly to the fact that their nature

30. Hewlett, A. W., Gilbert, Q. O., and Wickett, A. D.: Arch. Int. Med., 1916, **18,** 636.

is essentially the same. In uremia the kidney fails to fulfil its proper function, due to an anatomic lesion. In intestinal intoxication the same result is brought about through loss of fluid. Waste products normally excreted by the kidneys are retained because there is insufficient water for diuresis.

Similar to uremia, based on symptomatology, there are two groups of cases of intestinal intoxication. In one group convulsions, involuntary muscular movements, muscular twitching and coma are present. The onset is usually acute and the infant is not greatly emaciated. Diarrhea may be slight and is absent in some cases. Food or water is usually refused and is vomited if taken.

In the second group the onset is less acute, but occurs following vomiting and diarrhea of some days' duration. Convulsions rarely occur and the infant is somnolent or semistuporous instead of comatose. Wasting is very marked and the patient presents the shrunken appearance which is so characteristic of great loss of fluid.

In both uremia and intestinal intoxication acidosis is a frequent occurrence.

Aside from the question of acidosis, intestinal intoxication similar to uremia appears to be some form of poisoning. Whether this poison is a product which the kidney has failed to excrete, whether it arises from disordered metabolism or is elaborated by bacterial growth in the intestinal tract, is one of the fundamental problems with which we are confronted.

SUMMARY

In intestinal intoxication there is a marked increase in the nonprotein nitrogen and urea of the blood. This increase is not due directly to increased concentration of the blood from loss of water. The high nonprotein nitrogen and urea are due to defective kidney elimination.

The renal lesions in intestinal intoxication are not sufficient to account for the impaired elimination by the kidney. It is probably due to the fact that lack of water restricts the formation of urine. This condition is probably due to the following factors which may act singly or in combination: 1. The loss of water in the stools is so great that it is impossible for the infant to ingest sufficient fluid to replace the loss. 2. The patient refuses to ingest fluid or vomits practically all that is taken. As a result the tissues become dehydrated. The retention of nitrogenous waste products and the failure of the kidney to do its part in preserving the acid-base equilibrium results from the deficient secretion of urine. The oliguria may be due to the fact that the dehydrated tissues hold as much water as possible so that none is available for the formation of urine. Other factors, dependent mainly

on the loss of water, which may play a rôle are: 1, an increase in the concentration of blood colloids to such degree that their osmotic pressure is greater than the arterial pressure in the kidney; 2, a diminution in the total blood volume leading to decreased blood flow through the kidney.

The symptoms of intestinal intoxication are essentially those of uremia. The two conditions are similar in all essentials. In one, defective kidney function is due to an organic lesion; in the other it results from the negative water balance and consequent oliguria.

Acidosis plays a definite part in the symptomatology of intestinal intoxication, but the essential cause is probably some unknown toxic agency.

172 West Seventy-Ninth Street.

It is with pleasure that I acknowledge my great indebtedness to Dr. L. E. La Fétra for the use of material from his service and for his stimulating interest in the work. I desire to thank Dr. Charles Norris for examining and describing the kidney sections. To Dr. A. O. Gettler, pathologic chemist, Bellevue Hospital, I am indebted for much advice and assistance. My thanks are due to Dr. W. R. May for much assistance during the early part of the work.

EFFECT OF BODY POSTURE ON THE POSITION AND EMPTYING TIME OF THE STOMACH *

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There is yet much to learn about the baby's digestive apparatus. Any knowledge added, no matter how small in amount, will bring us nearer the desired goal of maximum information. This work was undertaken by us on account of the scarcity of reports especially concerning the motility of the child's stomach under the varying influences of posture.

Observations on Positions of the Stomach.—Sixteen observations of the effect of body posture on the position of the stomach were made in four cases. The influence of gravity both on the shape of the stomach and the position of the meal is well demonstrated in the illustrations. The gas bubble, no matter what the position of the stomach may be, always rises to the highest point of the stomach. We noted in one of our patients that at the age of 3 years the stomach approximated the adult type both in form and position.

Observations on Motility.—Thirty-three observations were made in twelve cases. Comparative examinations were made in the prone, supine, erect, right lateral and left lateral positions. In one of our cases the stomach was empty at the end of two hours, in two cases at the end of two and one-half hours, and in one case at the end of three hours. We found in some of the cases that the food did not enter the duodenum immediately following feeding. Active peristalsis was noted with the fluoroscope as early as the fourth month of life (Case 10821).

Technic.—In making the observations a Coolidge tube was used with 2 milliamperes of current, spark gap 6 inches, and distance from target to screen 20 inches. The method employed was by screen tracings, which were adopted in preference to the roentgenographic method, because they permitted of greater accuracy and certainty of results and a saving of time, permitting observations of respiratory movements on the stomach and a study of peristalsis. The opaque meal consisted of, in addition to the child's customary meal, barium sulphate, the amount varying from 100 grains in the youngest child of 6 weeks to 1 ounce

* Submitted for publication Jan. 31, 1918.
* Read before the Section on Diseases of Children at the Sixty-Eighth Annual Session of the American Medical Association, New York, June, 1917.

in a child 5 years old. The barium was thoroughly mixed with the food and in the cases of nursing infants the milk was withdrawn from the mother's breast in the quantity usually given by the mother to the baby as ascertained by weighing, barium mixed with it and the food given by bottle. In no instance was any untoward effect noticed in the children by reason of the addition of the barium. For the comparative observations of position of the stomach and motility, the meal and quantity in each individual case was the same. No attempt was made to test the exact time of emptying, on account of the variation

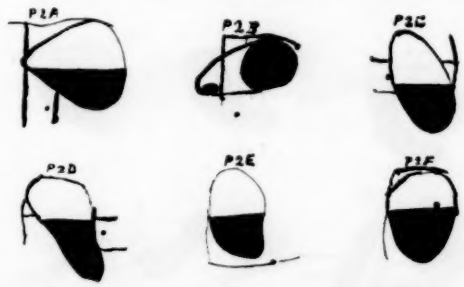

Fig. 1 (No. 10783).—Erect (P. A.) P2A; supine (P. A.) P2B; left lateral (P. A.) P2C; right lateral (P. A.) P2D; prone (right to left) P2E; supine (left to right) P2F.

Fig. 2 (No. 10816).—Erect (P. A.) P4A; supine (P. A.) P4B; erect (right to left) P4C; right lateral (right to left) P4D.

in the ages of the children and the composition of the food, but rather the relative emptying time as influenced by the body posture. The screen tracings of motility were all made at the end of a fixed interval for each individual child and the final tracing, irrespective of the position of the stomach during emptying, was made with the patient supine with the rays directed postero-anteriorly. These tracings were photographed and made into slides.

With regard to the emptying time, immediately following the termination of each feeding the child was placed in the posture under consideration and maintained in that position for a fixed interval. All

children observed were in good health and their gain in weight was not interfered with.

ANALYSIS OF CASES

1. Comparison of right and left lateral positions: four cases. Right showed increased motility.

2. Comparison of right lateral and supine positions: five cases.

3. Comparison of right lateral and prone positions: two cases.

4. Comparison of right lateral and erect positions: four cases.

In all of the foregoing the motility of the stomach was increased in the right lateral compared with the other positions.

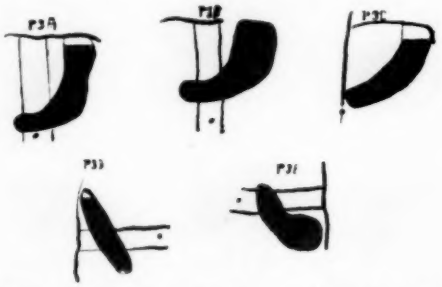

Fig. 3 (No 10028).—Erect (P. A.) P3A; supine (P. A.) P3B; erect (right to left) P3C; right lateral (P. A.) P3D; left lateral (P. A.) P3E.

Fig. 4 (No. 10895).—Right lateral, no tracing, empty; supine 1A; prone 1B.

Fig. 5 (No. 10821).—Supine 3A; Prone 3B; erect 3C; active peristalsis.

5. Comparison of left lateral with supine position: five cases. In four of these the left lateral position showed greater motility. In one case there was no difference.

6. Comparison of left lateral with prone position. Two observations in the prone position were discontinued because of colic, so that comparisons could not be made.

7. Comparison of left lateral with erect position: four cases. Two of these were in favor of the left lateral position and two in favor of the erect position.

8. Comparison of the supine with the prone position: five cases. It was necessary to discontinue two of the observations in the prone position on account of the extreme colic experienced by the infants. Three other cases showed an increased motility in the prone position. One of these three infants also suffered from colic, but the position was maintained.

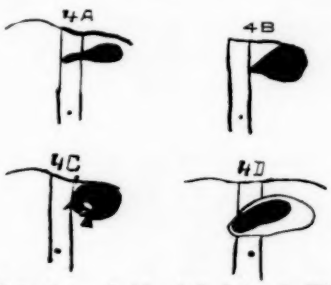

Fig. 6 (No. 10812).—Right lateral 4A; left lateral 4B; supine 4C; erect 4D.

Fig. 7 (No. 10623).—Right lateral, empty, no tracing; left lateral 5A; supine 5B; erect 5C.

Fig. 8 (No. 1100).—Right lateral 7A, empty; left lateral 7B, teething and fretful on day of left lateral; erect 7C.

Fig. 9 (No. 10830).—Right lateral 8A, empty; left lateral 8B; supine 8C.

9. Comparison of the supine with the erect position: six cases. Three of these were in favor of the supine position and three in favor of the erect position.

10. Comparison of the prone and erect positions: two cases. The prone posture showed increased motility as compared with the erect.

Table 1 shows the observations made on the position of the stomach, the posture of the child and the direction of the ray being indicated in each instance.

TABLE 1.—Observations on Position

Number	Age	Food	Quantity, Ounces	Barium Drams	Position and Direction of Ray				
					Erect	Supine	Prone	Right Lateral	Left Lateral
10783	4 mos.	Breast milk	4	2½	P. A.	P. A. S. D.	D. S.	P. A.	P. A.
10028	3 yrs.	Cow's milk	8	6	P. A. D. S.	P. A.	.....	P. A.	P. A.
10816	5 yrs.	Cow's milk	8	8	P. A D. S.	P. A.	.....	D. S.	
10812	4 mos.	Cow's milk, 33⅓%	4	2½	P. A.				

P. A. = postero-anterior; D. S. = dextrosinistral; S. D. = sinistrodextral.

TABLE 2.—Comparison of Residue in Different Postures *

Number	Age	Quantity, Ounces	Food	Interval, Hours	Barium, Drams	Relative Amount of Residue Left					Remarks
						Right Lateral	Left Lateral	Supine	Prone	Erect	
10812	4 mos.	4	Cow's milk, 33⅓%	2	2½	1	2½	2½	†	1½	
10623	7½ mos.	6	Breast milk	3	3	minus	1	2	...	2½	
11000	10 mos.	8	Cow's milk, 50%	2½	3½	minus	2½	...	...	1	Teething and fretful on day of left lateral
10830	15 mos.	8	Cow's milk, 50%	2½	4	minus	1	1½			
10783	4 mos.	4	Breast milk	2	2½	1	...	3	2	3¼	
10805	6 wks.	3	Cow's milk, 25%	2	100 gr.	minus	...	1½	1		
10921	2 7/12 yrs.	8	Cow's milk	3	6	...	1	1¼	†		
10926	2¼ yrs.	6	Cow's milk	3	4	...	minus	1¼	...	1	
10821	4 mos.	3½	Cow's milk, 50%	2	2½	...	...	2½	1	1¼	Active peristalsis
10915	9 mos.	8	Cow's milk, 75%	2	3½	...	...	1	...	3	

* One observation was made on each of two other cases, but as no comparative observations were made they were not tabulated.
† Observation discontinued because of colic.

Table 2 shows the observations made on motility, the relative amount of residue in the different postures being shown in each individual case.

CONCLUSIONS

1. The position of the stomach, and especially the position of the solid contents of the stomach, is influenced by body posture.

2. In one of our cases the age at which the adult type of stomach was reached was 3 years. (Case 10028.)

3. Motility of the stomach is most rapid in the right lateral position.

4. The supine position produces a comparatively slow motility.

5. Active peristalsis in the stomach was noted as early as the fourth month.

1776 State Street.

POLYCYSTIC KIDNEY IN AN INFANT*

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Cases of polycystic kidney observed in infancy, with necropsy findings, are still sufficiently rare to justify the report of the following case.

REPORT OF CASE

History.—E. S., of Syrian parentage, born July 1, 1916, of healthy parents. There were several other children in the family who were well and healthy. The family history was entirely negative. There was no history of miscarriages, no luetic history of any other kind and no known exposure to tuberculosis. The child was brought to the King's Daughters' visiting nurse clinic on July 28, 1916, then 4 weeks old.

Present Illness.—The mother said that she noticed before the child was 1 week old that its abdomen was unusually large, and that she thought it had grown since then. The child had appeared uncomfortable at times. There had been no vomiting. The stools had been regular, one to three per day, and on several occasions had contained small amounts of mucus. The child had nursed well and appeared satisfied with the breast. She thought the child passed more urine than most babies. The child was small and well developed, but emaciated. Otherwise than the stools there was nothing worthy of note.

Examination.—This showed a rather poorly developed child, though fairly well nourished; length, 19 inches; weight, 8 pounds 12 ounces; temperature, 98.6. The head appeared small (no measurements taken); the abdomen was quite large (17 inches in circumference); there were two masses present, one on each side of the umbilicus. These were apparent on inspection and palpation. They were distinctly nodular in outline and firm but movable, and appeared to arise from each side of the spinal column. They nearly filled both flanks and were dull to percussion, except when some folds of intestine, distended with gas, passed over them. The heart was negative. The liver was palpable about 1 cm. below the costal border. The spleen was not palpable. The von Pirquet test was negative and Wassermann ±, which in our clinic is disregarded unless there are other symptoms which lead to suspicion, and in that event another test is made.

The blood showed as follows: Hemoglobin, 60 per cent.; white blood cells, 14,000; red blood cells not counted; polynuclear cells, 55 per cent.; lymphocytes, 42 per cent.; eosinophils, 2 per cent.

The urine, which was examined repeatedly while the child was under observation, was uniformly negative, with the exception of one time, when a faint trace of albumin was reported. The urine, however, was never obtained in large enough quantities to determine the specific gravity, although the child always appeared to pass rather large amounts.

The subsequent history is of small moment. The child continued to nurse well and the milk was of good quality. Weighing before and after nursing showed that the child received from 2 ounces on admission to 4 ounces just before death. In spite of this the child did not grow in length or increase in weight. The latter, on the day before death, was 7 pounds 13 ounces. The temperature varied little and never exceeded 100 F. (during a mild attack of

* Submitted for publication Dec. 21, 1917.

Fig. 1.—Photographs of kidneys, not taken until hardened. Size of each when fresh, 10 by 7 by 3 cm.; weight, right, 200 gm.; left, 180 gm.

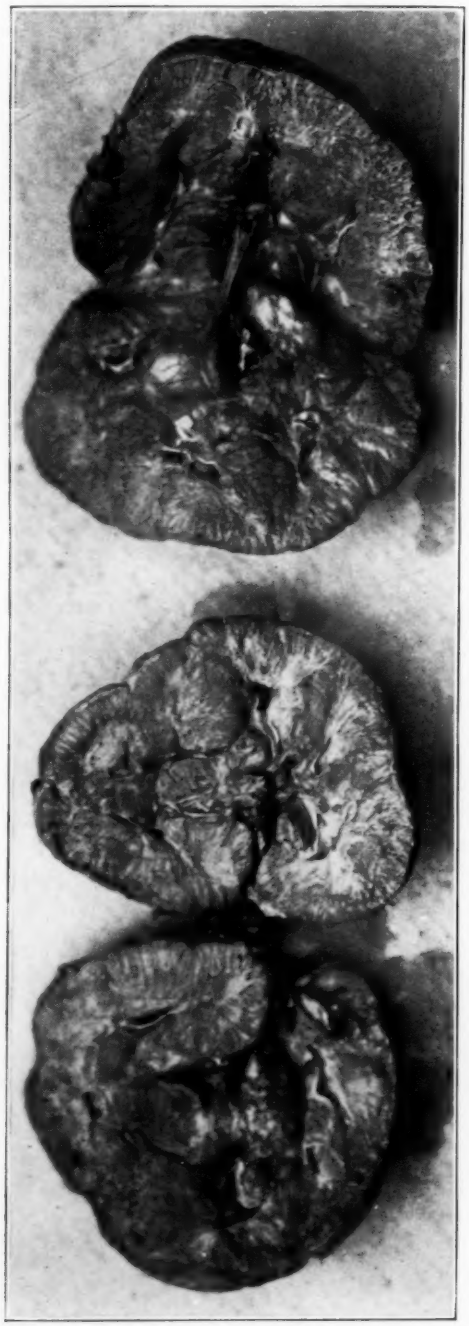

Fig. 2.—Photographs of kidneys laid open showing the gross pathology.

bronchitis). During the last months of life the child was very restless, appearing uncomfortable most of the time, and the mother thought there was pain.

Diagnosis.—From the negative von Pirquet, the very doubtful Wassermann and the good family history, both tuberculosis and syphilis were at once rejected. It seemed, therefore, that the diagnosis lay between sarcoma of the kidney and

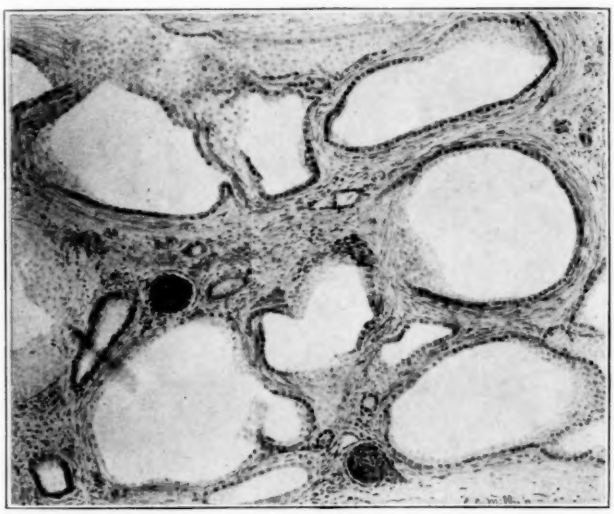

Fig. 3.—Drawing of a section of the cystic kidney, × 75. × 150.

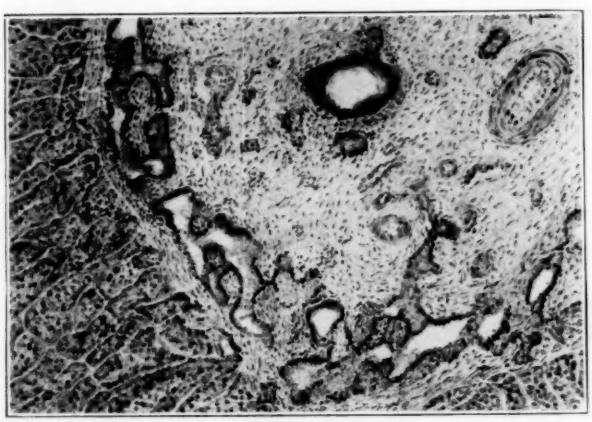

Fig. 4.—Drawing of section of liver, × 75. × 150.

polycystic kidney. Bilateral tumors of irregular outline, dating from birth, point strongly toward polycystic kidney. We therefore made this as the probable diagnosis. The parents suggested an operation, but we felt that this was not justified.

The patient was exhibited before the Norfolk County Medical Society as a case of polycystic kidney. The child died, Feb. 27, 1917, when 8 months old.

Necropsy.—This was performed by Dr. R. S. Kight. The pathological findings are as reported by Dr. Mary E. Roche, pathologist to the clinic.

A male child, aged 8 months; lenght, 20 inches; body very much emaciated; weight (just prior to death), 7 pounds 13 ounces; no subcutaneous fat. Heart not enlarged; abdomen distended. Lungs: Hypertrophic congestion over posterior surface of both lungs; no enlargement of bronchial lymph nodes. Abdomen: Colon distended with gas; peritoneum adherent to tumor masses in both sides of abdomen.

Kidneys: Enlarged, completely filling both sides of the abdominal cavity posteriorly from the liver to below the crest of ilium. Each kidney measured 10 by 7 by 3 cm., and was of grayish color. They weighed 200 and 180 gm., respectively. The external surface was rough, showing raised, lobulated areas. The capsules were thickened and adherent to the kidney substance. The kidneys were soft and elastic, the surface covered with cystic elevations, varying in size from 2 mm. to 1 cm. in diameter. On section, the cut surface was grayish, translucent, and yellowish watery fluid exuded from the cystic areas. White connective tissue bundles radiated from the pelvis toward the cortex. The cortex was about 1 cm. thick, with coarse striations running into the pyramids.

Liver: This organ did not extend below the costal margin. The surface was rough and nodular, resembling atrophic cirrhosis. On section the connective tissue was much increased, the capsule thickened, and cut with resistance. Microscopic frozen sections showed atrophied liver cells and much connective tissue.

Taylor Building.

ACUTE SYPHILITIC MENINGITIS IN AN INFANT TWELVE MONTHS OLD*

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Acute syphilitic meningitis has been recognized as a clinical entity since the year 1855,[1] but it was not until 1902[2] that the changes in the spinal fluid of this disease were observed. Ravaut,[3] writing in 1903, took the ground that syphilis in the secondary stage was a true septicemia, the skin and nervous system being principally affected. Whenever there were definite meningeal symptoms he found an increased number of lymphocytes in the spinal fluid.

The cytology of the spinal fluid was then studied rather extensively during the next ten years by the French writers. It was found that occasionally an increased number of lymphocytes was present in the spinal fluid, not only in the secondary stage of acquired syphilis, but also in hereditary syphilis (Tobler,[4] Ravaut and Ponselle[5]). The increase in the number of lymphocytes was found whenever there were meningeal symptoms, but occasionally when there were none.

A marked increase of the lymphocytes in the spinal fluid with a positive reaction for globulin suggested in these cases the presence of a syphilitic meningitis.

Sézary[6] has therefore divided the clinical manifestations of syphilitic meningitis, whether occurring in the acquired or hereditary type of syphilis, into three groups: (1) A latent form in which there are the general evidences of syphilis but no symptoms of meningitis; the spinal fluid in these cases is under increased tension; the cells are numerous and the globulin test positive. (2) A true meningitis: this condition is quite rare and presents the general symptoms and spinal fluid changes of an acute meningitis. (3) A more severe type which resembles an acute meningo-encephalitis: these patients have high fever, convulsions, marked rigidity of the neck and frequently localized paralyses, especially of the face and ocular muscles.

The great majority of cases of acute syphilitic meningitis, belonging to the second group described, have been observed in young adults.

* Submitted for publication Jan. 5, 1918.
* From the Babies' Hospital.

1. Reported by Bonnet and Goujat: Lyon méd., 1910, **114,** 549.
2. Milian, Crouzon and Paris: Bull. Soc. méd., Paris, 1902, **19,** 117.
3. Ravaut: Ann. d. dermat. et de syph., 1903, **4,** 537.
4. Tobler: Jahrb. f. Kinderh., 1906, **64,** 1.
5. Ravaut and Ponselle: Bull. et mém. Soc. méd. d. hôp., de Paris, 1906, **23,** 3.
6. Sézary, A.: Jour. méd. Franc., Par., 1913, **7,** 201.

In these cases the meningitis is usually secondary to an acquired syphilis. A few examples of acute syphilitic meningitis secondary to hereditary syphilis have, however, been reported.

Ravaut and Darré[7] were probably the first to report an example of this type with an extensive study of the changes in the spinal fluid: the infant was 3 weeks of age when first observed and presented the general manifestations of hereditary syphilis. During the first year the child had four separate and distinct attacks of meningitis. Spinal puncture greatly relieved the meningeal symptoms; in each instance the fluid was under increased tension, the lymphocytes numerous and the globulin test positive. During the second year the child remained healthy and several spinal punctures revealed a normal fluid.

A few years later Hutinel[8] stated that syphilitic meningitis occurs in infants, associated with such specific lesions as pemphigus, roseola and changes in the bones, liver and spleen. He quotes another example of this condition, observed by Ravaut, in an infant 3 weeks of age who presented scattered syphilids over the trunk and face, a hard liver and large spleen. There were observed numerous convulsions, a tense fontanel, and the spinal fluid showed a markedly increased number of lymphocytes. The diagnosis was confirmed by necropsy, numerous spirochetes being found in the exudate at the base of the brain.

REPORT OF CASE

History.—H. M., a male child, 12 months of age, was admitted to the Babies' Hospital June 7, 1916. The mother appeared healthy and denied having had syphilis; but the father, several years previously, had been treated for that disease. There had been four infants born at the seventh month of pregnancy before the birth of the patient. The first lived for five days; the second and third were stillborn, and the fourth lived but four days. The patient was born at term and appeared healthy. No history could be obtained from the mother, who was fairly intelligent, of any early manifestations of hereditary syphilis, or in fact any signs up to the time of admission. The infant was nursed for only five weeks, but later gained normally on modified milk mixtures, and at the time of admission weighed 18 pounds.

The first symptoms of the present illness occurred two weeks before admission; the child vomited several times a day and the bowels were constipated. Most of the food had been refused for a week, and for three days before admission there was a gradually increasing drowsiness. There was no history of fever or convulsions.

Examination.—On examination the child lay with head slightly retracted and breathing regularly. He took very little notice of his surroundings; was dull but not stupid. There were no lesions of the skin or the mucous membranes. The fontanel was tense but not bulging. There was definite but slight rigidity of the neck; pulse rate 100 and very slightly irregular; the spleen was not palpable, but the liver was felt at the costal margin; the epitrochlear glands were readily palpable; the knee jerks active and equal on both sides.

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7. Ravaut and Darré: Gaz. d. hôp., Par., 1907, **80,** 207.
8. Hutinel: Rev. gén. de clin. et de thérap., Par., 1913, **27,** 437.

The patient lived for four days; the drowsiness deepening into coma, in which condition he died without convulsions. The vomiting continued about once a day, The temperature remained practically normal until the day before death when it rose to 102 F. The blood count on admission was 17,700 leukocytes, 86 per cent. of which were polymorphonuclears and 14 per cent. lymphocytes. A second count four days later showed 18,200 with 71 per cent. polymorphonuclears and 29 per cent. lymphocytes. Three von Pirquet skin tests were negative.

About 15 c.c. of a slightly turbid spinal fluid were withdrawn by spinal puncture under moderately increased pressure. The cells numbered 650 per cm., 66 per cent. of these being lymphocytes. The globulin was moderately increased. Three subsequent spinal punctures gave practically the same results. Cultures made from the spinal fluid were negative in every instance and no tubercle bacilli could be found in the smears after a prolonged search.

On the third day after admission an examination of the eyegrounds by Dr. E. F. Krug revealed the presence of a typical syphilitic choroiditis. As a result of this finding the spinal fluid was examined for spirochetes. Smears were made from the sediment of centrifugalized specimens. Some were prepared by the India-ink method and others were stained with the Giemsa stain. Numerous spirochetes were found by both methods. They were confirmed by similar findings made on the following day from a fresh sample of spinal fluid. The Wassermann reaction was strongly positive in both the blood and spinal fluids. A single dose of diarsenol was given intravenously, but the child by this time was almost moribund and died the next day.

Necropsy.—(By Dr. Martha Wollstein.) The meninges were everywhere congested and the surface of the brain slightly compressed, especially over the left hemisphere. The pia was opaque in appearance and moderately edematous; more marked over the frontal lobes. There were small, irregular patches of grayish-white exudate covering the blood vessels in the sulci of the parietal and temporal lobes. This condition was most marked over the left temporal lobe and extending along the left sylvian fissure. There was nowhere seen any fibrinopurulent exudate as in meningococcus or pneumococcus meningitis, but the plaques resembled those sometimes seen in old meningococcus inflammations. The brain substance beneath showed considerable softening. The gray matter was studded with minute hemorrhages, and several small vessels showed the presence of minute thrombi. There was dilatation of the ventricles, with a slightly turbid fluid, especially on the left side. The floor of the posterior cornu of the left lateral ventricle showed many minute hemorrhages, two small thrombosed vessels and an early stage of softening. The right lateral ventricle was very slightly larger than normal and the floor of the anterior cornu showed some minute grayish-white plaques about 2 to 3 mm. in diameter.

Smears made from the exudate on the surface of the brain and from that in the ventricle all showed the presence of numerous spirochetes.

The heart was not enlarged; the endocardium of the left ventricle showed thickened grayish areas, more marked just below the aortic valve; the myocardium and valves appeared normal.

The liver was rather small; the capsule, especially along the upper surface, was thickened; there were also seen many subcapsular hemorrhages; the substance of the liver was firm, slightly fatty in some places and congested in others; the connective tissue was thickened throughout the organ. The lesion was essentially a syphilitic hepatitis.

DISCUSSION

The clinical picture presented by this infant closely resembled that of tuberculous meningitis. The gradual onset, the vomiting, the constipation and drowsiness were all typical of that disease. Even in spite of three negative tuberculin skin tests and a diligent search for tubercle

bacilli in the spinal fluid, it was thought probable that the case might still be tuberculous in origin. It was in the search for choroid tubercles that the first suggestion was obtained as to the true nature of the disease; and this led to an examination of the spinal fluid for spirochetes. From the presence of these in numbers the diagnosis was established.

It was now apparent that the symptoms differed in some important respects from those of tuberculous meningitis: the continued absence of fever and convulsions, the turbidity of the spinal fluid and the relatively small percentage of lymphocytes.,

In other turbid spinal fluids, pyogenic organisms are regularly found. None were present in this case, either by smear or culture.

Acute syphilitic meningitis in infants is a very rare condition and probably not more than half a dozen cases have been reported. In those cases which come to necropsy the spirochetes were demonstrated in the exudate at the base of the brain. But in the recent reviews of acute syphilitic meningitis by Bonnet and Goujat,[1] Miriel,[9] Jeanselme and Chevallier,[10] Desneux, Dujardin and Weil,[11] and Bonnet[12] not a single instance is recorded in which the spirochetes were demonstrated during life in this disease in infancy.

I am greatly indebted to Dr. L. Emmett Holt for permission to publish this report.

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10. Jeanselme and Chevallier: Rev. de méd., Par., 1912, **32,** 329.
11. Desneux, Dujardin and Weil: Jour. méd. de Brux., 1913, **18,** 175.
12. Bonnet: Lyon méd., 1915, **124,** 55.

PROGRESS IN PEDIATRICS

RÉSUMÉ OF LITERATURE ON TUBERCULOSIS IN CHILDREN, 1917 *

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MODE OF INFECTION

1. Weber, F. P.: Congenital Tuberculosis. Brit. Jour. Child. Dis., 1916, **13,** 321 and 359.
2. Park, W. H.: Channels of Infection and Methods of Transmission of Tuberculosis, New York Med. Jour., 1917, **105,** 777.
3. Klotz, O.: Portal of Entry and Route of Infection in Tuberculosis in Children. Pennsylvania Med. Jour., 1917, **20,** 811.
4. Opie, E. L.: Relation of Apical Tuberculosis of Adults to Focal Tuberculosis of Children and Adults. Jour. Exper. Med., 1917, **26,** 263.
5. Opie, E. L.: Focal Pulmonary Tuberculosis of Children and Adults. Jour. Exper. Med., 1917, **25,** 855.

F. Parkes Weber[1] reviews the literature on congenital tuberculosis, due to intrauterine infection by way of the placenta and fetal membranes. He says that genuine cases of congenital tuberculosis in human beings are undoubtedly rare, and it has been thought that they occurred only when the mother was in an advanced stage of tuberculosis, but more recent observations seem to show that placental tuberculosis may likewise develop when the mother's tuberculosis is not far advanced or is even latent or quiescent. The author's review includes thirty-three cases of true congenital tuberculosis, but he quotes the analysis of the subject by Pehu and Chalier who admit fifty-one cases as conclusively genuine and satisfying all critical demands. According to Pehu and Chalier, in cases of congenital tuberculosis in the infected fetus or infant there are generally tuberculous lesions to be seen in the organs, but in some cases, in spite of no pathologic-anatomic changes having been found, the fetal blood contains virulent tubercle bacilli. This latter condition is the status bacillaris of Honl and is to be distinguished from the actual presence of tuberculous lesions in the fetus.

Weber finds a difference of opinion as to the time of infection in these congenital cases. Pehu and Chalier say placental tuberculosis apparently does not occur until the fourth month of pregnancy. In this connection Pankow's work is of special interest. In twenty pregnant tuberculous women artificial abortion was brought about in the

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third or fourth month of pregnancy, and from all these cases fetal pulp was injected into guinea-pigs without giving rise to tuberculosis. Dufour and Thiers, however, report the instance of a young woman who died of tuberculosis in the third or the fourth month of pregnancy. The placenta appeared to be healthy, and examination for tubercle bacilli in it gave negative results; but the peritoneum of the fetus contained fluid, animal inoculation with which gave rise to tuberculosis.

W. H. Park,[2] discussing the channels and methods of transmission of tuberculous infection, says two types of tubercle bacillus cause the disease in man, the human and the bovine. In New York City during the four or five years that pasteurized milk has been more generally used there has been a marked reduction in the percentage of bovine infection among children, and on occurrence it has been found among children fed raw milk. Park thinks droplet infection is more important than that from dried sputum, and the dust of the rooms inhabited by tuberculous persons is only slightly or moderately infected with tubercle bacilli. However, when the sputum clings to lips, fingers or clothing of the patient, there is danger of the bacilli being conveyed to another person. When the contact is close, as when the mother nurses her infant, the danger is very great; when limited, as shaking hands, handling furniture or clothing, it is slight. Although living tubercle bacilli are found more or less abundantly in the feces of all patients with human or bovine open tuberculosis and although many reach the water supply, the danger from the water supply is slight.

O. Klotz[3] says that in spite of the tremendous amount of work done on all phases of the tuberculosis problem, there is no agreement on the question of the mode of infection. In order to throw more light on this subject he has searched for the tuberculous focus at 477 necropsies. A tuberculous process was met with in 170 cases of these 477, giving a percentage of 35. From his observations on these cases the author thinks there is no gainsaying the fact that the greatest incidence of tuberculosis is within the thorax, as compared with other parts of the body. This is true of all periods of life, even though in early childhood apparently a greater frequency of tuberculosis has been found in the bowel and its appendages. The closer analysis of the statistics of tuberculosis in childhood has recently indicated that the greater incidence of abdominal tuberculosis is not correct, when an impartial search is given to other parts of the body.

E. L. Opie[4] has attempted to show the relation of phthisis in adults to tuberculous infection in childhood. In order to do this he has studied the pathology of tuberculosis in children and adults and obtained data as to the frequency of infection among them. During

the first two years of life massive tuberculous lesions sometimes implicate a considerable part of one lung, but do not affect the apex more frequently than other parts. Lesions at this time exhibit no tendency to heal. After the end of the second year tuberculous lesions are usually small, seldom more than 1.5 mm. in diameter, and may be situated in any part of the lung substance. They may be designated as focal lesions and differ from the lesions of infancy only in size. They show, however, a tendency to heal, which is indicated by encapsulation of the caseous focus with fibrous tissue. The caseous material may undergo calcification and become surrounded by a fibrous capsule. The author found that nearly two thirds of all these tuberculous foci have been in contact with the pleural surface of the lung. The lesions are scattered impartially throughout the lungs. The most conspicuous characteristic of tuberculosis in children is the extent of involvement of the regional lymph nodes, but the author agrees with Ghon that the pulmonary lesion is primary and the lymphatic foci are secondary. Masses of greatly enlarged caseous lymphatic glands may occupy the hilus of the lung, in which is located the primary focus, and similar masses fill the spaces between the trachea and lungs or lie in the angle at the bifurcation of the trachea. As the age of the child increases there is less enlargement and caseation, and between the ages of 10 and 18 it is not uncommon to find small or calcified nodules in only one or two lymph nodes.

In adults tuberculous lesions of the lungs may be separated into two sharply defined groups: (1) lesions occupying the apexes of the lungs, tending to spread diffusely through the tissue of the apex and unaccompanied by caseation of the regional lymphatic nodes; (2) circumscribed lesions situated in any part of the lungs and accompanied by similar lesions of the regional lymph glands. In the lungs of adults who have died of disease other than tuberculosis this is the commonest type of tuberculous lesion. They have the distribution and characters of the circumscribed tuberculous lesions, which begin to appear after the second year of life and during later childhood and may be designated as focal tuberculosis. It is noteworthy that the incidence of focal tuberculosis increases continuously after the second year of life, and that at least 92 per cent. of all adults possess focal lesions. Focal tuberculosis is frequently fatal in early childhood, but after the tenth year it is rarely the cause of death. The existence of focal lesions does not preclude the occurrence of apical tuberculosis. Primary infection in almost all individuals who reach adult life occurs in childhood and has the characters of primary infection in animals, since it tends to implicate the regional lymph nodes. Koch showed that a secondary infection of an animal already tuberculous has a greater tendency to heal and does not extend to the regional lymph nodes, and this has

been confirmed by numerous observers. Apical tuberculosis usually exhibits the characteristics of secondary infection, since it pursues a chronic course and is usually unaccompanied by tuberculosis of the regional lymph glands.

Opie concludes, then, that focal tuberculosis of adults is identical with tuberculosis of childhood. It occurs in at least 92 per cent. of all adults. It may be acquired between the ages of 2 and 10, but in more than half of all individuals (in St. Louis) it makes its appearance between the ages of 10 and 18 years. Tuberculosis of childhood does not select the apexes of the lungs, is accompanied by massive tuberculosis of the regional lymph nodes, and exhibits the characteristics of tuberculosis in a freshly infected animal, while the tuberculosis which occurs in the pulmonary apexes of adults has the characters of a secondary infection. Almost all human beings are spontaneously "vaccinated" with tuberculosis before they reach adult life.

The following observations, E. L. Opie[5] believes, also indicate that apical tuberculosis of adults is not the result of infantile tuberculosis, but is caused by subsequent infection: (*a*) Apical tuberculosis does not have its highest incidence, in accordance with common belief, in early adult life when focal infections acquired in childhood are relatively fresh and active, but is more common in later life, when the focal lesions of childhood have in most instances completely healed. Most of these apical lesions of later life pursue a chronic course and are discovered at necropsy in individuals who have died from other causes; (*b*) the well characterized lesions of tuberculosis acquired in childhood and found in adults with apical lesions are almost invariably calcified and healed. The apical lesion is in most instances relatively fresh and caseous, while the focal pulmonary lesion and associated lesions of regional lymphatic nodes exhibit no evidence of activity; (*c*) in a large proportion of instances of associated focal and apical tuberculosis the focal lesion is in one lung, but the apical lesion is limited to the opposite apex. This relation affords no support to the view that tuberculous lesions may be transmitted to the apex by way of the lymphatics.

BACTERIOLOGY

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7. Griffith, A. S.: Human Type of Tubercle Bacilli in Tuberculosis. Brit. Jour. Tuberc., 1917, **11,** 160.

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10. Griffith, A. S.: Types of Tubercle Bacilli in Cervical and Axillary Adenitis. Lancet, London, 1917, **1,** 216.

11. Shimer, W.: Relation of Cow's Milk to Human Tuberculosis. Indiana State Med. Assn. Jour., 1917, **10,** 193.
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C. Y. Wang[6] has undertaken a study with the object of obtaining information as to the relative incidence of the human and bovine types of tubercle bacilli in the infection of man, irrespective of age and the nature of the tuberculous disease. The material was obtained from the pathologic department of the Royal Infirmary and Edinburgh Royal Hospital for sick children. One hundred and twenty-three strains of tubercle bacilli from 88 cases of tuberculosis were studied. All strains were found to conform in important respects to either the human or the bovine type of tubercle bacillus. In no instance was an atypical strain found. Of 68 cases of tuberculosis in adults, bovine tubercle bacilli were found in 7 instances, namely, from 1, of 29 cases of pulmonary tuberculosis, from 2 of 4 cases of abdominal tuberculosis, from 2 of 7 cases of generalized tuberculosis, and from 2 of 28 cases in which the only signs of tuberculosis were calcareous or caseous lesions. Three of the cases of bovine infection gave indication on postmortem examination that the path of infection was by way of the intestine. Of 20 cases of tuberculosis in children, bovine tubercle bacilli were isolated in 11 instances, namely, from 3 of 4 cases of abdominal tuberculosis, from 3 of 5 cases of tuberculous meningitis, and from 2 of 8 cases showing at necropsy no other evidence of tuberculosis than calcareous or caseous glands. In 9 of these cases of bovine infection the primary site of infection was in the intestine, as determined by postmortem examination. These bacteriologic findings confirm those of Fraser and Mitchell and emphasize again the great prevalence of bovine tuberculous infection in Edinburgh, especially among children.

Wang thinks the finding of a large percentage of tuberculous milk in Edinburgh explains only in part this high incidence of bovine tuberculosis there. He thinks the consumption of unboiled milk by the infant population is another very important factor. Investigation has shown that the diet of most children belonging to the working class consisted partly or wholly of cow's milk, and in only a small percentage was the milk boiled. Moreover, it was found that more children who were fed on raw milk gave a positive tuberculin test than those fed boiled milk.

In view of these facts Wang asserts that any measure resorted to in combating the disease should be directed not only against human spread of infection, but also against bovine source of infection. An adequate supervision of milk supply failing, the most efficient way of

safeguarding against the bovine type of tubercle bacillus is to subject all cow's milk for consumption to the process of boiling.

A. S. Griffith[7] in summarizing the work of the British Commission on Tuberculosis found that in 930 cases of tuberculosis occurring at all ages the bovine bacillus was the infecting organism in 18.17 per cent. One hundred and ninety-six, or 34.2 per cent., of these cases occurred in children up to 5 years; 265, or 26.8 per cent., in children between 5 and 10 years; 127, or 12.6 per cent., in children between 10 and 16 years, and 341, or 5.9 per cent., in individuals above 16 years.

M. P. Ravenel[8] reviews the work done in the matter of transmission of bovine tubercle bacilli to human beings and regards it as a mistake to emphasize too strongly that the danger from bovine infection is greater in early life. He has been forced to the conclusion that infection of adults with the human tubercle bacillus is much less common than was formerly believed and thinks it possible that further studies, considering the relative proportion of human and bovine infection, will show that adults are infected with the bovine tubercle bacillus relatively as frequently as with the human. Moreover, Ravenel does not believe that the portal of entry of the tubercle bacillus can be told from what is considered the oldest lesion — for example, that cases are of inhalation origin when the pulmonary lesions are the most advanced in the body. In animals it has been conclusively shown that pulmonary tuberculosis can be easily produced both by feeding and by injection of tubercle bacilli directly into the stomach, and the oldest lesions are found in the lungs after infection of known intestinal origin. It seems almost certain that the same thing may take place in children.

A. Philip Mitchell[9] has attempted to ascertain the frequency of primary tuberculosis of the faucial tonsils and its relation to other tuberculous affections, especially to tuberculosis of the cervical lymph nodes. His study has consisted of examination of tonsils removed from children affected with tuberculosis of the upper deep cervical glands, and of hypertrophied tonsils removed from children with no clinical evidence of tuberculosis of the lymph nodes or other structures. The methods employed were histologic examination of the tonsils and inoculation of tonsillar tissue into guinea-pigs. The author thinks that histologic examination of the entire tonsil is a reliable diagnostic method, but he employs animal inoculations, also, to meet the criticism of those who maintain that foreign substances in the tonsils are frequently the cause of lesions identical with those produced by tuberculosis. Moreover, animal inoculations were necessary to determine the relative frequency of the human and bovine type of tubercle bacillus present in tuberculous tonsils.

There were 106 cases in which the tonsils were removed at operation for tuberculosis of the cervical glands. Of these, 51 cases were in children under 5 years, 49 cases in children between 5 and 15 years, and 6 cases were in adults. In 41 cases there were undoubtedly tuberculous lesions in the tonsils and 38 of these were in children. Inoculation tests were made in 92 of the 106 cases and positive results obtained in 20 cases. In 16 cases the bovine bacillus was obtained and in 4 the human type of tubercle bacillus was obtained.

There were 100 cases in which the faucial tonsils were removed for chronic hypertrophy and 9, or 9 per cent., yielded positive results when inoculated into guinea-pigs. The bovine bacillus was present in 4 cases, and the human in 2 cases, and in the other 3 cases the type was not determined.

Mitchell thinks the interpretation of these bacteriologic findings impossible without considering the source of infection. In a previous investigation he examined 406 samples of milk and in 82, or 20 per cent., he found tubercle bacilli. Children being large consumers of milk, it is quite clear how contaminated milk may be to them a frequent source of infection. In this connection it must be mentioned that 90 per cent. of the children under 5 years of age were bottle fed infants. Among children with tuberculous cervical adenitis, human source of infection seems very frequently absent. In not a single instance of bovine tonsillar infection in this series was there a history of pulmonary tuberculosis in other members of the household.

Mitchell draws the following conclusions from his study: 1. Tuberculosis of the upper deep cervical glands develops from a primary focus in the faucial tonsils much more frequently than is generally supposed. 2. Primary tuberculosis of the tonsils can be recognized only by the aid of the microscope and by inoculation experiments. The lesions are found immediately under the surface epithelium and near the mouth of the lacunae and in relation to the deeper portions of crypts or deep in the tonsils close to the capsule. The first mentioned site furnishes the greatest number of examples. 3. Hypertrophied faucial tonsils are the seat of primary tuberculosis, though rarely, as compared with tonsils from cases of tuberculous cervical adenitis. 4. Experimental results indicated that in Scotland primary tuberculosis of the faucial tonsils must be attributed to the drinking of milk from tuberculous cows, rather than to the inhalation of the tubercle bacillus conveyed by dried sputum or moist spray of a consumptive patient. 5. Bovine and human types of tubercle bacilli are present in the crypts of a small percentage of children without demonstrable tuberculous lesions either in the tonsils or elsewhere. 6. Tonsillectomy is essential in all cases of tuberculous cervical adenitis in chil-

dren. 7. The prognosis is very slightly influenced in children in whom the faucial tonsils and cervical glands are simultaneously affected with tuberculosis. 8. The difficulties associated with the reform of the milk supply and the lengthened period which must elapse before it becomes possible to obtain milk free from tubercle bacilli demand some means of rendering milk safe. The only safeguard is to be had in sterilization by boiling.

Since his last report on bacteriologic findings in cervical adenitis, A. S. Griffith[10] has studied fifty-two additional cases in order to ascertain the type of infecting organism. In seventeen of the cases no tubercle bacilli were found and inoculations into guinea-pigs were negative. In thirty-five cases cultures of tubercle bacilli were isolated either from the original material or from material obtained after the inoculation of guinea-pigs. In fifteen of the thirty-five cases the cultures showed the bovine tubercle bacillus. In nineteen cases the human bacillus was isolated and in three the strain was atypical. The author's figures show that in children under 10 years cervical gland tuberculosis is caused more frequently by the bovine than by the human type of tubercle bacillus, for three fourths of the cases in children under 10 years yielded the bovine type of organism. In persons over 10 years infection of human origin is more common, for in only one third of the individuals from 10 to 20 years was the bovine organism obtained, and in rather less than one fifth of the cases in persons over 20 years.

W. Shimer[11] has studied the relation of cow's milk to human tuberculosis. According to the author's statistics, one dairy cow of every ten has tuberculosis (i. e., in Indiana). Hence, if every dairy man kept ten or more cows and mixed the milk, all of the milk would contain tubercle bacilli. Cows rarely suffer from tuberculosis of the udders, and Shimer thinks the chief source of the tubercle bacilli is the feces. Most market milk contains manure, and there are always tubercle bacilli in the manure of cows with tuberculosis, as they invariably swallow their sputum. Cream is one of the greatest sources of danger. Cream contains a concentration of tubercle bacilli and is made into butter. The interval of time which elapses between the production and use of cream and cream products is so short that the bacilli retain their virulence. As long as raw milk from tuberculous cows, or its products, continues to be used, living organisms will find entrance into the human organism. The bovine type of bacillus is responsible for about 1 per cent. of infection in man and 5 per cent. of infection in children under 15 years of age.

S. J. Wang and F. Cooley, during the last year and a half at Sea View Hospital, Staten Island, N. Y., examined the breast milk of

twenty-eight tuberculous women for tubercle bacilli. There was no apparent mammary disease or suspicion of such in any case. The specimens of milk were obtained from these women twice each week, from 3 to 5 c. c. being gathered by breast massage, under aseptic precautions, for each test. All specimens were examined within two hours after they were withdrawn from the breast. An ordinary smear was first stained for tubercle bacilli, then the remainder of the specimen was reduced with weak antiformin solution, and the resulting sediment was examined for tubercle bacilli. Specimens from each of the last fifteen of the series were injected into guinea-pigs intraperitoneally; the guinea-pigs were killed six weeks later and tuberculous changes sought.

All the specimens injected into guinea-pigs were negative. No tuberculous changes were found, and no effects of any kind from the milk injections occurred in the animals.

Altogether there were about 450 microscopic examinations of specimens taken bi-weekly from the whole series of twenty-eight cases. These were all negative except one, which the writers think was questionable.

Some observations were also made on two guinea-pigs that were fed breast milk from two tuberculous women. The milk from these women, both of whom had normal, full-term deliveries in the hospital, was fed to the animals three times a day for one month. As much milk as possible was obtained for each feeding, the amounts varying from 10 to 40 c.c. A small amount of lettuce and bread also was fed them. This experiment was carried out to ascertain whether the animals became tuberculous and, if they did not, whether they gained weight and throve on these feedings. If these specimens of milk contained toxic substances, it was thought that the guinea-pigs might show some effects from the daily ingestion of such relatively large amounts. Both guinea-pigs had lost weight at the end of the thirty days. Soon after necropsy was performed on the guinea-pigs and no evidence of tuberculosis was found in either animal.

The authors feel that the negative results of these experiments seem to indicate that tubercle bacilli are infrequently found in the breast milk of tuberculous women who have no mammary disease. The possibility of infection from such milk is probably slight, but it is very likely best to inderdict nursing in every instance, because of the additional dangers, that of infection during the intimate relationship of the mother and the nursing child, the possibility of toxic substance in the milk, and the bad effects of nursing on the mother. An exception might be made in the instance of a mother with a closed case of tuberculosis, although it is often difficult to distinguish between a closed and open case after pregnancy and labor. The tuberculous

woman undergoes a profound strain before and during childbirth, and it frequently takes a long period of observation to ascertain whether her disease has been activated.

SYMPTOMATOLOGY

13. Barbier, H.: Tuberculosis in Infants Under Two. Paris méd., 1917, **7,** 109.
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16. Commarata: Tuberculous Meningitis Simulating Multiple Sclerosis, Abstr. Am. Rev. Tuberc., 1917, **1,** 121.
17. Bonaba, J.: Tuberculosis of the Cerebellum. Abstr. Arch. de méd. d. enf., 1916, **19,** 649.
18. D'Espine, A., and Demole, V.: Tubercles of the Pons. Arch. de méd. d. enf., 1917, **20,** 355.
19. Ash, R. L.: A Contribution to the Diagnosis of Spinal Cord Tumors in Childhood. Am. Jour. Dis. Child., 1917, **13,** 487.
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Canelli, A.: Miliary Tuberculosis During the First Weeks of Life. Abstr. Arch. de méd. d. enf., 1917, **20,** 375.

Porter, L.: Tuberculosis in Childhood with Unusual Manifestations. California State Jour. Med., 1917, **15,** 303.

Bordet, E., and Ovidio, R.: Tuberculous Meningitis in Infants. Semana méd., 1917, **24,** 385.

Morrison, J. R.: Tuberculous Meningitis. Kentucky Med. Jour., 1917, **15,** 277.

Bernstein, H. S.: A Case of Tuberculous Meningitis. Rhode Island Med. Jour., 1917, **1,** 68.

For ten years H. Barbier[13] has been interested in the question of tuberculosis in infants and has sought for this disease at all necropsies. One of his interns found a proportion of 32 per cent. of deaths from tuberculosis in infants under 2 years of age. Another statistical report showed tuberculosis in 39 per cent. of children dying from all causes. But Barbier thinks statistics furnished by necropsy reports are lower than those which represent the morbidity of tuberculosis in infants, for he thinks that all infants below 2 years inoculated with tuberculosis do not die, as is proved by finding among older children lesions which evidently originated at a very early date.

As to the frequency of ulcerative forms, the author found eighty-four cases at 194 necropsies, and adding these personal observations to those published by different authors, Barbier found in a total of 766 necropsies on tuberculous infants 220 cases of cavities, or 29 per cent. Cavities rarely form before the third month and they usually

occur between the sixth and eighteenth month. The frequency of these ulcerative lesions goes to prove the great morbidity of tuberculosis in infants, and Barbier thinks that often symptoms like dyspnea, febrile attacks and cough in so-called atrophic infants are but manifestations of the evolution of a tuberculosis.

M. S. Reuben[14] reports a case of tuberculosis in a nine weeks old baby following ritual circumcision. On the eighth day the child had been circumcised by a mohl, who aspirated the wound by means of a glass tube. Within a week the wound of the circumcision had healed. Five weeks later the mother noticed a swelling in the right groin and brought the child to the writer for treatment. Physical examination showed that the inguinal glands in the right groin were enlarged, the mass being about the size of the small finger; there was also swelling of the left inguinal glands, but not to the same extent as on the right side. Examination of the penis revealed four small tuberculous masses on the anterior surface of the circumcision scar. On palpation of these masses one obtained the feeling not unlike that of shot under the skin; they felt hard and indurated. The largest of these tuberculous masses was excised and microscopic examination showed the tissue was infiltrated with numerous tubercles and diffuse tuberculous inflammatory material. The von Pirquet reaction of the infant was positive. The mohl was found to be suffering from advanced tuberculosis and his sputum was loaded with tubercle bacilli.

Reuben reviewed the literature on this subject and found reports of forty-two cases of tuberculous infection following circumcision. He thinks the incidence of this infection is much greater, as many cases have probably not been reported. The treatment is early excision of the tuberculous tissue of the penis and of the inguinal glands on both sides.

The rarity of Addison's disease among children makes a case reported by J. Comby[15] of especial interest. The case was that of a 13 year old girl whose father had died of pulmonary tuberculosis eight years before. The necropsy showed old pleuritic adhesions, but no tubercles in the lungs or tracheo-bronchial glands. The right suprarenal capsule was much enlarged, nodular and softened. On section a caseous fluid escaped and it was impossible to distinguish any normal tissue. The kidney of the same side showed several yellow tubercles. The left suprarenal was enlarged, but less so than the right, and contained a number of tubercles. The liver and spleen were increased in size and also contained tubercles.

Commarata[16] describes a case of tuberculous meningitis simulating multiple sclerosis in a 3 year old boy. Six months before consultation he developed a tremor of the right hand, which was worse during the

day. Three months later the boy walked with a tremulous, spastic gait and sensation was found to be lost in the right leg. There was an intention tremor so marked that he could not raise a glass to the lips. No evidence of meningitis was present and a diagnosis of multiple sclerosis was made. Some weeks later he was seized with fever, headache, vomiting, stiff neck and a convergent strabismus, which in a few days terminated in convulsions. Lumbar puncture gave a fluid under increased pressure containing tubercle bacilli. There was some temporary improvement after the puncture, but death occurred shortly.

J. Bonaba [17] discusses three cases of tuberculoma of the cerebellum in children. He describes symptoms and gives the necropsy report in each case.

A. D'Espine and V. Demole[18] report a case of tubercles of the pons in a 7 year old boy. From the symptoms a diagnosis was made of a tubercle in the eminentia teres of the right side of the pons. Necropsy showed tracheobronchitis, caseous pulmonary tuberculosis, caseated tracheobronchial glands, ulcerative intestinal tuberculosis, multiple conglomerate tubercles of the brain, cerebellum, and bulb, recent miliary tuberculosis and acute tuberculous meningitis. The findings in the pons were especially interesting. Two tubercles were situated in the right eminentia teres, one in the center of the pyramidal tract, which had almost destroyed the point of origin of the right oculomotor nerve and greatly injured the facial. This lesion explained the paralysis of these two nerves. The second tubercle was situated in the center of the right pyramidal bundle, but only separated the fibers and did not destroy them, a fact which explained the exaggerated reflexes and clonus and the absence of hemiplegia.

R. L. Ash[19] reports an unusual case of tuberculoma of the spinal cord in a 19 months old baby, giving it as a contribution to the study and diagnosis of spinal tumors in childhood. The clinical diagnosis was intramedullary or extramedullary tumor of the spinal cord, compression myelitis and meningitis, probably of tuberculous origin. The child died and necropsy confirmed the diagnosis. There was a general tuberculosis, a tuberculoma of the cerebrum and a tuberculoma of the spinal cord. This latter was olive-shaped, 2.5 by 1.2 cm. in size, and was situated extramedullary in the cervical enlargement of the spinal cord. It was grayish-white and caseous in appearance and microscopically was composed of typical tuberculous tissue. Of special interest in this case is the fact that a tumor of the spinal meninges, which was diagnosed during life, was the first manifestation of a generalized tuberculosis in a child of 19 months. Xanthochromia with massive spontaneous coagulation and pleocytosis was an attending syndrome.

W. E. Ladd[20] discusses the subject of tuberculous cervical adenitis

in children. He says the commonest portal of entrance of the infection is the tonsil, though occasionally the adenoids, teeth, ear or skin of the face and scalp are the source, and that further investigation should be undertaken to give a more definite answer to the question of the disease originating from bovine or human type of tubercle bacillus. If it becomes firmly established that milk is responsible for the majority of infections, it would seem possible greatly to reduce their frequency by securing nontuberculous milk supplies.

F. Harbitz,[21] since his last article in 1905, has investigated further the question of tuberculosis of the lymph nodes and has paid particular attention to the general form of the disease, its frequency in children and adults, its origin and its importance as a cause of death. He says that it is not well known that tuberculosis of the lymph nodes may be a general disease, that is, one which affects the entire lymphatic glandular system. It may be encountered incidentally in postmortem examinations or, as is more commonly the case, it may occur with extensive and, as a rule, eventually fatal cases of tuberculosis, when it is the older and primary lesion and thus indirectly the cause of death. The author's observations were based on 2,906 necropsies, 2,489 of adults and 417 of children. He divides tuberculosis of the lymph glands into seven groups, which include tuberculosis of the bronchial, cervical and abdominal glands, combinations of these three groups, and last and most important, general lymph gland tuberculosis. In this important group were included sixty-one cases, thirty-two of adults and twenty-nine of children. Of the cases in children twenty occurred during the first year of life and in almost all there was a history of tuberculosis in the immediate relatives, usually in the parents. In all these, extensive tuberculous processes were found in the internal organs, as well as in the glands, so that it was impossible to trace the connection between the two processes, but the process in the lymph nodes was clearly the most marked and oldest. The lymph nodes of the neck, of the thorax and of the abdomen were extensively affected, occasionally also those of the axillary and inguinal regions. The process in the neck was a descending one, most marked above and extending down to the supraclavicular space, where the glands were smallest. In the thorax the process was an ascending one, the glands were smallest above around the trachea, while around the bifurcation and pulmonary hilus they were largest. In the abdomen the tuberculosis was usually limited to the mesenteric nodes, or retroperitoneal nodes, where they formed large masses around the aorta, celiac axis or in the hilus of the liver or spleen. In general it did not appear that there was a continuous extension from one group of glands to another, but the impression was rather that a repeated infection had taken place by different paths,

especially as the process appeared to be of different ages, old in some glands, recent in others which had no direct connection with the first. This could be explained by exposure to infection at different times, both by inhalation and swallowing, and the possibility of reinfection was often established by obtaining a history of contact with a phthisical patient. As to the mode of extension, Harbitz thinks that after one or more infections of different groups there is extension along the lymph vessels and then a dissemination through the blood to all groups of glands, until it is impossible to trace the route or mode of infection. Pulmonary tuberculosis appears to be the cause of death in about one-half the cases of general lymph gland tuberculosis. Particularly in older children, but not rarely in the first years of childhood and in infancy, the tuberculosis in the lungs assumes the form of phthisis in adults with cavity formation. Less frequently there is an apical tuberculosis due to extension to the lungs from the nodes in the upper part of the mediastinum or supraclavicular regions. Tuberculosis of the intestinal tract is the cause of death in about one fourth of the cases. In these instances the primary lesion developed presumably in the abdominal lymph nodes. Miliary tuberculosis, or tuberculous meningitis is also the cause in about one fourth of the cases, especially in instances of tuberculosis of isolated groups of glands.

A. T. Jones[22] reports nine cases of tuberculous glands of the mesentery, three in children. Operation was performed to relieve surgical symptoms and at the operation the primary cause of the trouble was found to be disease of the mesenteric glands. Jones believes that the tuberculous mesenteric gland is often a primary disease of the true tuberculous type, but the bovine type is undoubtedly present in many children without producing symptoms, the glands remaining quiescent or having a tendency to subside. As a rule, it is impossible to make a correct diagnosis before operation, unless there are glands which can be felt through the abdominal wall or by the finger in the rectum. There are two clinical types: (*a*) a slightly progressive one, generally with palpable glands; (*b*) an acute fulminating type, frequently simulating, and impossible to differentiate from, appendicitis. The prognosis in the subacute stage is good without operation. In the acute stage exploratory laparotomy should be performed, but the glands not removed, unless there are definite indications of adhesions or ulceration, or unless the large size of the mass produces much pain or obstruction. From Jones' experience tuberculous glands of the mesentery may present no symptoms until breaking down begins in the glands, and after that there are symptoms of tuberculous peritonitis, intestinal obstruction, or acute appendicitis. He says that in children and young adults with a history of right sided abdominal pain with or

without palpable masses, inflamed mesenteric glands should be considered a possibility.

C. M. Du Pan[23] describes an unusual case of tuberculosis of the mesentery in an 8 year old boy.

TUBERCULOSIS OF THE TRACHEOBRONCHIAL GLANDS

24. Floyd, C., Boutwell, H. K., and George, A. W.: The Diagnosis of Thoracic Adenitis. Internat. Clin., 1916, **3,** 130.
25. Lapham, M. E.: Tuberculosis of Infants. Southern Med. Jour., 1917, **10,** 465.
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27. Bloom, C. J.: D'Espine's Sign, A Valuable Aid in the Diagnosis of Pulmonary and Tracheobronchial Tuberculosis in Childhood. New Orleans Med. and Surg. Jour., 1917, **59,** 748.
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C. Floyd, H. K. Boutwell and A. W. George[24] discuss the pathology, symptoms and diagnosis of enlarged thoracic glands, a term they prefer to bronchial glands, the one now in use, as it includes the groups of glands not only about the root of the lungs, but also on either side of the trachea. Enlargement of thoracic glands has been noted in many infections, not only in tuberculosis and Hodgkin's disease, but also in the acute contagious diseases of children, as measles, scarlet fever, pertussis, and still more recently in the common acute bronchial colds. Most observers, however, are of the opinion that tuberculosis is the most common cause of enlargement of these glands. The writers believe that the symptomatology of enlarged thoracic glands is still one of considerable uncertainty and obscurity. Lassitude, slight elevation of temperature, more or less constant thoracic pain, especially in the interscapular region, and a brassy cough are the symptoms most often noted. But the writers have failed to detect any constant symptoms in this condition. When, however, there occur persistent elevated temperature and pulse and harsh, dry cough, anemia and lack of normal development, without other explanatory condition, the possibility of thoracic adenitis should be considered. The diagnosis has given rise to a great variety of opinions as to the value of certain signs commonly associated with its presence. The most important ones are enlargement of the superficial thoracic veins, irregularity of the pupils, the so-called Eustace Smith sign, an increase in normal area of dulness, extending outward on either side of the sternum, D'Espine's sign, vertebral dulness or resistance, or both, below the first dorsal spine, which does not change with full inspiration. One or more of these signs, supplemented by positive evidence of fluoroscopic examination and roentgenograms, are generally considered pathognomonic of tracheobronchial adenitis.

The authors' observations have led them to believe that in children whose bronchial glands on the right side are considerably enlarged, there not infrequently occur at the right apex definite signs of consolidation, such as dulness, increased resistance, limited expansion and bronchovesicular breathing. Prolonged observation, clinical and by means of the roentgen ray, have shown in these cases no apical lesion and, with subsidence of the bronchial nodes, there is entire disappearance of these signs. The condition seems to be due to a retraction of the apex, together with a reflex limitation of its function. The authors think that no single sign should be depended on, but in the majority of instances, where parasternal or paravertebral dulness occurs, the diagnosis is correct. D'Espine's sign is of importance, but to a slighter degree than formerly thought. It may, however, be the first clinical sign to appear and may be the only one in acute respiratory infections. The other signs, while they occasionally occur in extensive involvement of the thoracic glands, are too infrequently present to be relied on. No study of bronchial or hilus region is complete without repeated roentgen ray examination, but even here the shadows present may be confused or accompany other conditions, and reliance should not be placed on roentgen-ray examination alone. The authors believe far too little stress has been laid on thoracic adenopathy and that with the advent of more exact methods of study of diseases of the chest the importance of enlarged thoracic glands will be recognized.

M. E. Lapham[25] divides the symptoms of tuberculosis of the bronchial glands in infants into those due to pressure and those due to absorption of the toxins. Death may occur if the caseating glands perforate the air passages and fill them with caseous material, or if the infectious material is carried to other parts of the lung and induces caseous or bronchopneumonia, acute miliary tuberculosis, typhobacillemia of Landouzy, or meningitis. The symptoms of pressure are due either to irritation of the pulmonary nerves lying on the surface of the trachea and bronchi or to obstruction to the passage of air. Symptoms suggestive of enlarged bronchial glands are high-pitched, explosive paroxysmal attacks of coughing or a cough resembling the bellowing of a young hound. Often the cough is the first and only symptom for a long time; again it is preceded or overshadowed by the expiratory dyspnea. The expiratory dyspnea is the most constant and reliable symptom of obstruction of the air passages. Frequently there is a bitonal cough, due to pressure on one recurrent nerve and lack of symmetrical functioning of the vocal cords. Vomiting may prove a distressing symptom. Bronchial râles are very common and characteristic.

Symptoms caused by absorption of the toxins are vague; the vaso-

motor, gastrointestinal and hematopoietic systems are chiefly affected. It is possible that the vasamotor system may show the first effect of the toxins, which cause a fall in blood pressure and relaxation of the vessel walls, resulting in sluggish circulation in the gastro-intestinal and hematopoietic systems. Spasmophilia and chorea, which frequently precede tuberculosis, may be manifestations of vasomotor disturbances. The functional activities of the gastro-intestinal tract may be stimulated or depressed by the tuberculotoxins. Hyperacidity is a result of overstimulation. The child regurgitates food, is restless and fretful, but does not lose appetite. Anacidity, on the other hand, causes lack of appetite, constipation and apathy. There is loss of weight and, finally, marked atrophy. There is, however, nothing specific or suggestive of tuberculosis in the disturbances of nutrition resulting from tuberculous toxemia. This is true also of the disturbances of the hematopoietic system. There is hardly a disease of this system, from simple chlorosis to pernicious anemia, which cannot be simulated by tuberculous toxemia.

Tuberculosis of the bronchial glands is not necessarily a wasting or cachectic disease. Fatal perforation and such consequences of perforation as meningitis occur invariably in well-nourished infants.

H. M. Rich[26] says the diagnosis of tuberculous bronchial glands is made by considering four groups of facts: (1) history of exposure; (2) presence of symptoms otherwise unexplained; (3) physical signs, including the roentgen-ray findings, and (4) the specific reaction to tuberculin.

An infant living in contact with an open case of tuberculosis practically never escapes infection. A history of exposure is strong predisposing evidence in favor of tuberculous infection having taken place. The symptoms are somewhat indefinite. The earliest symptom is the decline of customary activity, with increased irritability. Loss of appetite and failure to gain weight follow. Many times the writer has noted repeated fleeting attacks of pallor. The temperature range is but slightly disturbed. Cough may or may not be present. It is usually brassy, paroxysmal and ineffective. Change of voice, hoarseness, and attacks of paroxysmal dyspnea may be noted. In the early stage none of the usual signs of phthisis are observed. The findings point to increased mediastinal activity, shown by the presence of D'Espine's sign and of dulness on direct percussion over the vertebrae. A third sign is a variation in the intensity of inspiration in the lower interscapular spaces. It may be heard on either side and is usually quite marked. The findings should always be substantiated by roentgen-ray examination, by which the increased density of the mediastinum can be easily demonstrated. Specific reactions may be

obtained by the von Pirquet test for the first three years of life, by the Calmette test in later life, if no contraindications exist. A positive result with either test means an active tuberculous process. A negative test may be disregarded in the presence of other strong evidence of bronchial gland tuberculosis. The early stage of a mediastinal tumor is perhaps the most difficult condition to differentiate from bronchial gland tuberculosis. The symptoms and physical signs are at first the same, but gradually change as the tumor grows larger. More frequently, however, a distinction must be made between bronchial gland tuberculosis and convalescence from pneumonia. Physical signs of mediastinal density may persist after the signs in the lungs have cleared and fever and malaise may continue for a considerable period. A tuberculin test here is of considerable value. Measles followed by enlarged bronchial glands may also offer difficulty in differential diagnosis.

C. J. Bloom's[27] experience with D'Espine's sign covers a series of seventeen cases, in which the sign was positive and a diagnosis of enlarged tracheobronchial glands was made before the roentgen-ray examination. From his study, Bloom wishes to impress the following facts: In infancy the anteroposterior diameter of the chest is relatively small and the glands are normally enlarged, so alteration in their size can be detected and is an aid in diagnosis. D'Espine's sign is a valuable aid in the diagnosis of tracheobronchial tuberculosis, but a positive D'Espine sign only shows an enlargement and does not signify that it is due to a tuberculosis. The sign is most significant under 10 years of age.

DIAGNOSIS

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The following outline for the diagnosis of tuberculosis in children is formulated by J. A. Miller and B. H. Waters[28] for the National Association for the Study and Prevention of Tuberculosis.

In the history record should be made of exposure to infection (especially if prolonged), delayed convalescence from any illness, malnutrition, underweight or loss of weight, cough, expectoration, hemorrhage, pain, pleurisy, dyspnea, night sweats, digestive disturbances and ear discharge.

Important physical signs are persistent and persistently localized râles, additional abnormal signs elicited by the usual methods of examination, any gland, joint, bone, muscular, cutaneous, ocular or aural abnormalities. Essential for diagnosis of pulmonary tuberculosis are distinct persistent or persistently localized adventitious sounds in the chest. Temperature over 99 F. by mouth recorded twice a week for a month and not otherwise to be explained. A positive tuberculin test. Exceptionally, in the absence of adventitious signs, a diagnosis of tuberculosis can be made in the following instances: (1) A positive tuberculin reaction with an unquestioned and otherwise unexplained hemoptysis, with or without a positive roentgenogram; (2) a positive tuberculin reaction in children under 3 or 4 years of age without constitutional symptoms, and in older children with frequent cough or rapid pulse or fever, and a roentgenogram which shows unmistakable mottling in the pulmonic field. No patient with fever and persistent physical signs should be considered free from tuberculosis until the tuberculin test has given a negative reaction three successive times. Examiners are reminded that undue importance should not be ascribed to slight vocal and respiratory modifications or to slight alterations in the percussion note so frequently present in children, especially at the apexes.

For the diagnosis of forms of tuberculosis other than pulmonary there must exist suggestive physical signs or constitutional symptoms or both, a negative Wassermann and a positive tuberculin test.

On a study of the case records of 200 children in a sanitarium for tuberculosis, H. D. Chadwick and R. Morgan[29] summarize the essentials in the diagnosis of this disease. They emphasize the importance of symptoms indicating tuberculin absorption, namely, weakness, undue fatigue, fever, poor appetite, failure to gain, or loss of weight

and nervous irritability. Symptoms of local involvement are cough, hoarseness and occasionally streaked sputum. The usual physical signs are dulness in the interscapular region radiating into the apexes at the back, frequently not elicited in front. There may or may not be changes in the respiratory sounds. Râles may or may not be present. Symptoms, both constitutional and local, together with a history of exposure, are to be given greater weight in making a diagnosis of active tuberculosis than the presence or absence of physical signs. Percussion is more important than auscultation. A thickened area in the lung or region of the bronchial glands does not in itself mean active tuberculosis. It may be a healed lesion that needs no treatment. Such thickening may also be caused by other diseases than tuberculosis. The child showing constitutional symptoms, even without local signs of disease in the chest, should be considered suspicious, kept under careful observation, and subjected to hygienic treatment in the home. Signs in the chest without constitutional symptoms indicate an old inactive infection that needs no treatment. Individualization and common sense must be used, all the factors in the case weighed and, with experience as a guide, few errors in diagnosis will be made.

M. Fishberg[80] discusses the diagnosis of pulmonary tuberculosis in children of school age. He believes it exceedingly rare at this age, and that when it does occur it is of the same type as in adults. Moreover, the physical findings and symptoms are practically the same as when the disease occurs in adults. Thus, children with pulmonary tuberculosis (if the disease is active) have cough, fever, night sweats, tachycardia, and emaciation. The cough may be mild or severe, may be paroxysmal or croupy, or not unlike whooping cough. The fever may be of any type, but it must not be forgotten that instability of temperature is very common and that fever alone is not to be considered pathognomonic of tuberculosis. Excitement, excessive exercise, or a slight gastric disturbance may elevate it. Also moderate elevation of temperature is very frequently due to focal infections of the nose and throat. Night sweats are only significant when they occur during the early morning hours. The pulse rate is an important diagnostic criterion. Active tuberculosis of the lungs may be excluded, when a child under 10 years has a pulse rate of less than eighty per minute. Tachycardia is almost invariably the rule in phthisis of children. Enlargement of the supraclavicular glands is also of great diagnostic significance. It is nearly always due to tuberculosis of the apex of the lung of the affected side. With any or all of the above symptoms pulmonary tuberculosis should be suspected, but no diagnosis made unless the lesion is localized by physical exploration of the chest. In pulmonary tuberculosis of children the lesion is almost invariably

localized at the apex, and statements made by some authors to the effect that it is found at the base or in the region of the hilus result from a confusion of disease of the tracheobronchial glands with disease of the pulmonary parenchyma. Pulmonary tuberculosis should be diagnosed in a child with lesions in the lower lobes, only when tubercle bacilli are found in the sputum, or when all other possible causes have been excluded. Bronchiectasis and multiple abscesses of the lung may give signs similar to those of tuberculosis. In many children suffering from adenoid vegetations of the nasopharynx there is impaired resonance in one of the apexes, usually the right, with bronchial or bronchovesicular breathing. Inasmuch as there is cough and often fever or loss of weight, the diagnosis of tuberculosis is likely to be made. Similar physical signs occur also in children with valvular heart disease. The roentgen ray is of immense value in diagnosis, if properly interpreted. In pulmonary tuberculosis in children the opacities will be found in the parenchyma of the apex, as in adults. Roentgen-ray findings, however, without constitutional symptoms do not justify a diagnosis of pulmonary tuberculosis. As regards the findings of tubercle bacilli in the sputum of children with pulmonary tuberculosis, Fishberg has found them in nearly all his cases. The tuberculin test he says is of no value in children over 4 years, as it only indicates tuberculous infection, not tuberculous disease.

In J. Signorelli's[31] experience the physical signs were the most important factor in the diagnosis of pulmonary tuberculosis in children. Next was the roentgen-ray examination, which has never failed to corroborate a lesion found clinically, while in obscure cases it has often pointed the way to a conclusion. The von Pirquet test applied three consecutive times, he found, gave a positive reaction in 85 per cent. of children with tuberculosis, while children with nontuberculous lesions always failed to react. D'Espine's sign he found present in 80 per cent. of tuberculous and in 15 per cent. of nontuberculous patients. The finding of tubercle bacilli in the sputum was an absolutely indisputable sign. Signorelli emphasizes the importance of not depending on one mode of examination or on one single examination in making a diagnosis, even though it might appear conclusive.

A. Lankester[32] has attempted to find some physical test, easy of application to schoolchildren on a large scale, which could be relied on to give an indication of the extent and prevalence of tuberculosis in the environment from which the children come. He thought that as a very large percentage of enlarged cervical glands are due to tuberculous infection, he might be able to determine a true correlation between the percentage of children showing enlargement of these glands and the number of cases of phthisis in the community to which

they belong. After compiling and studying statistics, however, he has come to the conclusion that the gland index method needs to be further safeguarded before it can be regarded as suitable for general adoption as a measure for tuberculous prevalence. The reasons for this conclusion are the element of possible variation due to a personal factor in the examiner, and to the fact that tuberculosis is only one among several causes of glandular enlargement.

J. H. Mason Knox, Jr.,[40] reports the results of a study of the von Pirquet cutaneous test for tuberculosis in a series of children on whom careful necropsies were performed. The test was made as a routine measure with Koch's old tuberculin. During the period of investigation, from November, 1912, to April, 1917, there were 2,940 children admitted to the hospital and there were 750 deaths. Necropsies were performed on 324 children. Two hundred and fifty-six, or 80 per cent., were found free of tuberculosis, and sixty-eight, or 20 per cent., were found to have tuberculous lesions. Of the 256 cases having no tuberculous lesion, the tuberculin test had been made in 172 instances and was negative without exception. Of the sixty-eight cases in which tuberculous lesions were found, the von Pirquet test had been performed in sixty-one. Of these it was positive in forty-five and negative in sixteen. The negative cases were carefully analyzed. In twelve instances the patients had a rapidly advancing, widespread miliary tuberculosis, in two instances a tuberculous meningitis, in two, advanced pulmonary tuberculosis, and in one, a tuberculous peritonitis. Knox concludes from these results that the cutaneous tuberculin test as described by von Pirquet is a most reliable aid in the detection of tuberculosis in children; that a positive reaction invariably indicates a tuberculous focus in the body, and that a persistently negative reaction establishes the fact that there is no lesion except in those extremely sick patients, where the presence of tuberculosis can be readily established by physical examination.

G. Lindberg[34] has applied repeated skin tuberculin tests to 129 children from 1 to 12 years in the hospital and sanatorium with which he is connected. The tuberculin skin test was applied to each arm and repeated after a week's interval. The reaction was measured in both the axial and transverse diameters twenty-four hours after the test and a week later. When neither diameter was over 5 mm. the reaction was recorded as negative. Of the 129 children, 33.3 per cent. showed a much more pronounced response to the second test than to the first. In 60 per cent. the response was weaker in the second than in the first; in 6.7 per cent. there was but slight difference.

Lindberg divides the patients into three groups—those with active, those with probable and those with nontuberculous lesions. Intensifi-

cation of the reaction, or positive sensitization, occurred in only 5.3 per cent. of the thirty-six cases in the first group; in 28.5 per cent. of sixteen in the probable group, and in 78 per cent. of the last group.

The results of the research testify that with inactive tuberculosis the response to the repetition of the tuberculin skin test is more pronounced than at the first test, while the reverse is the rule with active tuberculosis. The attenuation of the response to a second application of the test has thus a favorable instead of an unfavorable significance.

S. Pisani[35] reports his results with the cutaneous tuberculin test, when the injection is made in the skin over the affected viscera. In patients having unilateral renal tuberculosis without other active lesions he has observed that the cutaneous reaction is markedly positive in the lumbar region on the side corresponding to the affected kidney and negative on the other side. The reaction in the skin of the arm may be positive or negative.

In patients suffering from tuberculous peritonitis and in those with tuberculosis of the adnexa, the cutaneous reaction in the skin of the abdomen is very marked, while on the arm it is negative or only slightly positive.

In patients with incipient pulmonary tuberculosis, localized in the apex, with no fever the cutaneous reaction is more precocious and intense in the neighborhood of the affected part. The opposite is true with advanced lesions and in patients with high temperatures.

In patients with a bilateral pulmonary tuberculosis, recent or old, febrile or apyretic, the cutaneous reaction is more intense on the side of the less advanced lesion, a true paradoxical reaction.

In patients suffering from pulmonary tuberculosis with a therapeutic pneumothorax, the cutaneous reaction diminishes without becoming completely negative on the side of the pneumothorax; on the other hand, it becomes positive on the opposite side. If therapeutic intervention, however, has been performed early for a purely unilateral lesion, the reaction usually disappears on both sides.

In patients affected with pleurisy with effusion, the cutaneous reaction varies; usually the fluid hinders the manifestation of the cutaneous reaction.

Pisani concludes that the regional cutaneous reaction is merely a phenomenon of reaction in a region containing lymphatics which drain a tuberculous lesion. Its diagnostic significance is identical with that of the ordinary cutaneous reaction. Its essential characteristic is its greater sensitiveness.

H. J. Gauvain[36] applied the von Pirquet test with human and bovine tuberculin to children suffering from tuberculosis of the bones and joints. He wished to ascertain whether the reaction was constantly

present in this form of tuberculous disease; if not present, under what circumstances the reaction would not appear; whether it could be decided by using both human and bovine tuberculin for the test that the patient was suffering from tuberculosis of human or bovine origin; whether the degree of reaction would be an indication of the severity of the infection. The author employed Koch's old tuberculin prepared from the human type of bacilli, and his tuberculin prepared in the identical way from bacilli of bovine origin. The tuberculins were applied to suitable skin scarifications in dilutions of 1:64, 1:16, 1:14, and in full strength, each in approximately equal bulk and controlled by inoculation of the same quantity of sterile normal saline solution. In all, eighty cases were investigated. Local reactions to both human and bovine tuberculin were invariably present in patients from whom tubercle bacilli were isolated from the local lesions. The local reactions to human and bovine tuberculin, however, were found to be essentially similar. In twenty-three the reactions were so nearly equal that it was impossible to decide which was greater. In twenty-one cases the reaction to human tuberculin was somewhat greater than to bovine, and in twenty-five the reaction to bovine was slightly more marked than to human. In four cases the reaction to human tuberculin was markedly greater than to the bovine, and in seven the bovine was markedly greater than to the human. It was therefore impossible by the nature of the reaction to the tuberculin employed to differentiate the type of tubercle bacilli with which the patient was attacked. Gauvain found that patients who were weakly and cachectic, irrespective of the severity of the local tuberculous lesion, reacted feebly, while patients who were strong showed an intense or mild reaction, irrespective of the local lesion. No guide to prognosis could be found by comparing the reactions produced by the weaker and stronger solutions of tuberculin.

M. L. Brocq[37] reports an instance of lichen scrofulosorum developing around an intradermal tuberculin reaction. The patient, a 13½-year-old girl, entered the hospital April 19, 1917. For five years she had been frail and delicate and had suffered from enlarged cervical and submaxillary glands. During the last two years these had greatly enlarged, and, when the child entered the hospital, had formed voluminous masses on either side of the neck. There was also evidence of enlargement of the tracheobronchial glands. A month before entrance there had appeared on the anterior part of the thorax, the abdomen, in the hypogastric region on the lower part of the back, in the sacrolumbar region and in the region of the deltoids, lesions typical of lichen scrofulosorum. At the same time on the anterior surfaces of both legs were discrete, larger lesions, which were diagnosed as papu-

lonecrotic tuberculids. On entrance to the hospital an intradermal tuberculin test was made with one drop of a 1 to 10,000 solution of tuberculin. In forty-eight hours there was a strong local reaction and an elevation of temperature to 38 C. The center of the reaction was of an opaline tint, at least 1 cm. in diameter; the periphery was swollen and bright red. The following day there was a bulla in the center and two days later there formed a small superficial scab, which dropped off in fifteen days. Ten days after the formation of the scab there appeared around the intradermal reaction a bright red eruption having all the characteristics of a lichen scrofulosorum. Between the central scar and the eruption was a zone free of lesions, corresponding to the erythematous zone area which surrounded the central scar the first few days of the reaction. On the twenty-third of May a second intradermal reaction was made in the left thigh, which was followed by a reaction as strong as the first, although no eruption appeared. Following this second test the eruption on the arm seemed to fade. The two points to which the writer calls particular attention are the appearance of the lichen scrofulosorum around an intradermal tuberculin reaction and the development of a zone 2.5 cm. in diameter around the reaction where no eruption formed. He quotes several reports of eruptions following injection of tuberculin, but none which resembled this.

M. Kashara[38] believes he has discovered a specific diagnosis of tuberculous meningitis, by a focal reaction to tuberculin. After the removal of a certain quantity of cerebrospinal fluid by lumbar puncture for cytologic examination an intradural injection is made of from 0.01 to 0.002 mg. of Koch's old tuberculin diluted with 0.5 to 1 c.c. of physiologic salt solution. After six, twelve or twenty-four hours a cytologic examination is again made of the fluid, which is obtained by lumbar puncture, and a comparison made with that previously obtained. In this way the author examined nine cases and found that after the tuberculin injection there was an increase in the number of cells in general, and chiefly a remarkable appearance of red blood cells, a considerable increase in the lymphocytes, and a moderate increase in the polymorphonuclear cells. Moreover, in cases of tuberculous meningitis the cerebrospinal fluid after the injection is turbid and occasionally yellow in color. Kashara found no change in the cerebrospinal fluid after the injection of tuberculin in cases of epidemic meningitis and of chronic hydrocephalus.

J. Golay[39] has observed in the Children's Clinic at Geneva many cases of meningismus and of meningitis with a lymphocytosis which simulated tuberculous meningitis, and he has found that by a chemical examination a diagnosis can be made with more certainty than by a

cytologic examination, and more rapidly than by a bacteriologic examination. He emphasizes the importance of differentiating these conditions, especially in view of the benign character of meningismus and of the fatal outcome of tuberculous meningitis. Golay studied the spinal fluid in twenty-six cases of tuberculous meningitis and found in twenty-three a high albumin content, that is, ranging between 1 or 2 gm. per thousand, instead of the normal 0.1 or 0.2 gm. per thousand. In other forms of meningitis and meningismus it ranges between 0.1 and 0.3 gm. per thousand. For determining the amount of albumin the author used either the silver nitrate or neutral chromate of potassium test. Moreover, Golay found that the determination of the amount of chlorids was of great value in making the diagnosis. In the cases of tuberculous meningitis the chlorids ran very low. Instead of the normal 7.25 to 7.40 gm. per thousand they ranged between 5.5 to 6.5 gm., while in cases of meningismus and meningitis they remained within the normal limits.

J. Leffler[40] has made a study of the feces of 100 tuberculous children and has analyzed the literature on the finding of tubercle bacilli in the stools of children with tuberculous processes of the respiratory tract. Examination of the feces by the Reh method gave positive results in 16.4 per cent. of the cases, most of these being children of 11 to 14 years or infants under 1 year. The author believes that the examination of the feces should be undertaken as a routine procedure along with other diagnostic methods. He thinks it is especially valuable in infiltrating pulmonary tuberculosis of young children, where sputum containing tubercle bacilli is obtained only with difficulty, if at all.

PROGNOSIS

41. Hemplemann, T. C.: Prognosis of Tuberculosis in Infancy. Am. Rev. of Tuberc., 1917, **1,** 99.

42. Hemplemann, T. C.: Frequency of Tuberculids in Infancy and Childhood and their Relation to Prognosis. Arch. Pédat., 1917, **34,** 362.

43. Schwab, J. B.: The Diazo Reaction No Guide in the Prognosis of Tuberculosis in Children. Nederl. Tijdschr. v. Geneesk, 1917, **1,** 1010.

In regard to the prognosis of tuberculosis in children, T. C. Hempelmann[41] says that evidence is accumulating which proves that a certain number of children with pulmonary tuberculosis even in the first year of life do recover, and that this number could be increased if as much effort and care were expended on them as on those who contract it later. The author has studied the mortality of 130 cases of pulmonary tuberculosis in the first two years of life and has arranged the cases in three tables. Table 1 shows the number of children known to have died, the age at the time the diagnosis was made, and the interval elapsing between this and death. In this group

were sixty-four, of whom thirty-seven were less than 1 year old at the time of diagnosis, and twenty-seven were in the second year of life. Forty-six, or 72 per cent., died within three months after diagnosis. As many of these infants were brought to the hospital moribund, these figures give no reliable indication of the rate of progress of the disease. Eighteen infants lived at least three months after the diagnosis was made, nine lived over six months, seven over nine months, three more than a year, and one a year and a half.

Table 2 shows the number of children living at the time of the last note on the history sheet, their ages at the time of the diagnosis of tuberculosis and the length of time they were under observation. There were sixty-six cases in all. Thirty-one were followed less than six months, thirty-five more than six months. Thirty infants were observed for one year or longer, and some observed for periods of four to five years. Only two of these showed symptoms referable to the lungs when last seen, while seven gave other evidence of tuberculosis. Of these thirty, ten were under 1 year of age, when the diagnosis was made, and only one showed active tuberculosis at the time of this report. The other twenty infants were between the ages of 12 and 24 months when the diagnosis was made, and only one showed evidence of pulmonary disease at the time of the report, although six others showed other evidence of tuberculous disease.

Table 3 gives the mortality statistics of children who lived for at least one year. Under 1 year of age the mortality was 78.7 per cent.; from 1 to 2 years it was 57.4 per cent., and for 2 years, 68 per cent.

T. C. Hemplemann[42] has made an effort to ascertain the relation of tuberculids to prognosis in children. Here and there in the literature he has found the statement that tuberculids are of very grave prognostic import in the tuberculosis of childhood, and that their presence is an indication of general miliary tuberculosis. Hemplemann's material consisted of 130 cases of pulmonary tuberculosis in infants under 2 years of age, thirty of whom showed papulonecrotic tuberculids, and ten cases of tuberculids in children between 2 and 12 years. In all but one of the forty cases there was evidence of lung or tracheobronchial lymph node involvement in addition to the tuberculids. Of the forty children, thirteen are known to have died, eleven of these being in the first year of life and the other two in the second. Eleven children were observed for a period of at least one year after the occurrence of the tuberculids and were doing well when last heard from. Five of these were in the first year of life, five in the second, and one in the fourth. Of the five under 1 year, three were observed for two years or longer, two for three or longer, and one for five years. Of the five in the second year of life, two were observed for three

years and one for four years. One other child, 3½ years old when the tuberculids were discovered, was living at the time of the last note on the history, over two years later. In addition to these children there were sixteen more living, but they were observed for less than a year, and are classified in a separate group because of the uncertainty of their fate. From these statistics the author concludes that tuberculids bear no direct relation to prognosis, as some of the children under observation had showed tuberculids four or five years.

J. B. Schwab[43] comments on the difficulty of deciding the prognosis of tuberculosis in children. She studied the diazo and urochromogen reactions in the urine to see whether any light could be thrown on the subject. The children studied were under observation for various periods of time, some only a few days, others as long as seven years. Among them there were 23 with tuberculous meningitis; 15 with generalized tuberculosis; 5 with pulmonary and peritoneal tuberculosis; 10 with tuberculous peritonitis; 33 with pulmonary tuberculosis, and a number with tuberculous pleurisy and glands. The diazo reaction was constantly negative in 55, including 35 progressive and fatal cases, and constantly positive in 27, of which 23 have since proved fatal. The urochromogen reaction ran parallel to the diazo with a few exceptions and did not seem more sensitive than the latter. In 7 cases the diazo varied from positive to negative and clinically the prognosis in this group was always dubious or grave. In short, the article may be summarized by the statement that the diazo reaction is not a reliable guide for the prognosis of tuberculosis in children.

PROPHYLAXIS

44. Combe: Prophylaxis and Prevention of Generalization of Tuberculosis in Infants. Le Nourrisson, 1916, **4,** 347.
45. Moor, F. C.: Tuberculous Disease of Children. Southern Med. Jour., 1917, **10,** 300.
46. Kirkwood, R. M.: The Child and the Tuberculosis Problem. Pediatrics, 1917, **29,** 46.
47. Kerr, J.: Phthisis and School Children. Pediatrics, 1917, **29,** 184.
48. Quimby, J. P.: The Preventorium for Children at Farmington, New Jersey. Modern Hosp., 1917, **8,** 177.
Minor, C. L.: Importance of Control of Childhood Infection in the Crusade for the Eradication of Tuberculosis. Southern Med. Jour., 1917, **10,** 122.

Combe[44] discusses at length the prophylaxis of tuberculosis in infancy. He says that infection during the first 18 months means death within six or eight months, and so must be prevented at any cost. Prophylactic measures include prevention of infection both by the bovine and human bacillus. To prevent bovine infection milk must be obtained from healthy, tuberculin-tested cows; otherwise it must be boiled or pasteurized. The greatest danger to the infant comes

from human infection — from some tuberculous member of the family — and measures to prevent this kind of infection are expensive and difficult to carry out in the homes of the poor and middle class, since the child must be kept from contact with the tuberculous individual and with objects contaminated by the bacilli. Phthisical mothers are the chief source of infection. They must not nurse their infants, not only because of the toxins the milk contains, but because of the great danger of multiple reinfection from the intimate contact of mother and babe. Tuberculous parents should never kiss their infants, and should limit contact to strict necessity, and that never without washing and disinfecting their hands. They should disinfect their mouths many times a day and hold a handkerchief before the mouth when talking, coughing or sneezing. To prevent infection from contaminated objects, all toilet and table articles should be boiled regularly after use. Soiled linen and clothes should be thrown into boiling water and pressed with a very hot iron. Floors should never be swept, but dusted with a cloth dipped in turpentine. Walls and floors should be washed frequently with antiseptics. The infant should never be allowed to crawl on the floor, or only on a freshly laundered sheet in a railed space. All toys, rubber nipples, etc., should be boiled each time they are given to the child. For the most part prophylaxis in the home is inapplicable and not efficacious and resort must be had to removal of either the patient or the infant. The author is of the opinion that the only means of preventing tuberculosis in infants is to found asylums where infants of tuberculous parents can be placed directly after birth. In France, Germany and Switzerland institutions of this kind are already established.

In case the infant has become infected, prophylactic measures must be taken to prevent generalization of the disease. This can best be done by increasing the resistance of the infant, by change of climate, by proper diet and heliotherapy. The author prefers subalpine to alpine climates for these infants and is not quite sure of the advisability of sending them to the seashore. He thinks heliotherapy is a great aid in raising the resistance, and uses not only sun baths but artificial rays (actinic), declaring the results with the artificial ultraviolet rays to be identical with those obtained with the sun's rays. As to diet, he believes that a great many tuberculous infants suffer from a toxic dyspepsia, with inability to digest fats, so they should be fed a fat-free milk to which has been added malt, farina and Soxhlet's sugar. In some instances they thrive better on albumin milk. A wet-nurse should be procured if possible.

In a paper on tuberculous disease of children, F. C. Moor[45] discusses first the frequency, the symptoms and the signs of the disease

and then emphasizes the importance of prophylaxis. He says the first decade of life is the period of greatest susceptibility to the infection, and the prophylaxis of tuberculosis in childhood is the most important proposition confronting the medical profession. Moor thinks the first requisite for the proper institution of preventive measures is a complete census of cases of tuberculosis and the enforcing of a law that all new cases be reported. In connection with these reports there should be collected data as to the home conditions of the patients, the number of rooms available for occupancy, the size of the family, and especially the number and ages of the children. These data should be arranged on a unit basis, and with such an arrangement one district nurse to each unit could make the rounds often enough to keep in touch with conditions in each family and to a certain extent combine the duties of a visiting tuberculosis nurse and child welfare worker. Other points to be emphasized are ample protection of all children under 5 and prevention of massive infection, which is sure to occur when there is active disease in either parents or some other member of the household. In families in which ignorance and poverty or a bedridden mother makes home conditions hopeless, there is nothing to be considered but the removal of the younger children to a preventorium, the establishment of which is one of the first problems.

A second and less important requirement in preventing infection is the control of bovine tuberculosis. This can be done by uniform state laws or, better still, by federal laws.

In addition, the author touches on the importance of improving the general physical condition of the child, especially during school age, and he suggests a school medical adviser as well as a school medical inspector. Every child who is anemic, under weight, scrofulous, or otherwise below par should be given the advantage of open air schools and receive especial care from the medical supervisor.

To the end of preventing tuberculosis in the child, R. M. Kirkwood[46] suggests a number of measures. Very important is the establishment in existing sanatoriums of maternity departments properly equipped and in charge of competent obstetricians, or the establishment of especial maternity sanatoriums or open-air pavillions in existing maternity hospitals, where pregnant women approaching term can be cared for under ideal conditions for a pulmonary invalid; where they can be delivered by a technic most careful to conserve strength, and where the new-born babe can be immediately removed from the tuberculous mother and fed by a nontuberculous wetnurse or by artificial means.

Other measures suggested by the author are the examination for tuberculosis of midwives, obstetric nurses and nurse maids; the sys-

tematic performance of the von Pirquet test on all children; the establishment of preventoriums for children in the pretuberculous stage; the passing of laws prohibiting the marriage of the tuberculous; careful hygiene of homes and schools; proper feeding of children; instruction of school teachers in regard to facts about tuberculosis and its prevention.

According to J. Kerr,[47] statistics in England show that in the five years before school age and in the years after school age the mortality rate from phthisis among females is continually decreasing, as compared with that of males, while at school age the mortality among boys goes down progressively faster than among girls. Similar statistics have been collected on the continent. The writer thinks this difference in the phthisis mortality between the two sexes represents a difference in vitality and preventable illness, and he emphasizes the necessity of a more natural life for both boys and girls, instead of the cloistered life of the old schoolroom.

J. Palmer Quimby[48] describes the Tuberculosis Preventorium for Children at Farmingdale, New Jersey. He says that this institution was organized primarily for the care of poorly nourished, underfed children, exposed to tuberculous infection in their homes, who had already contracted tuberculosis, as a positive tuberculin reaction showed, but who had no open lesion. At the preventorium over 100 children are accommodated. They are kept for an average period of four and a half months, so that the institution provides annually for nearly 600 children. In addition to a reception pavilion where all children are quarantined for three weeks in order to prevent infection of the large group, there are four open air shacks, each accommodating thirty-two children, a small infirmary, school buildings, a large administration building, with a dining room which seats all of the children, and, last but not least, 170 acres of land in the sandy pine belt, over which the children roam and play. As children are accepted between the ages of four and fourteen years, it is necessary to give school instruction. There are three teachers, and the two-hour school period provided has proved sufficient to keep the children up to their public school grades.

During the stay of the children at the preventorium the condition of their homes is looked into and improvements instigated. Every six months after discharge the children are visited in their homes and their physical condition and the surroundings noted.

The executive committee of the preventorium determined to help the general tuberculosis campaign by giving employment to tuberculous patients with arrested disease. At the time of writing this article there were fifteen people of this class there and the plan as a whole has proved successful. Also in connection with the preventorium there

has been built a nursery for the care of infants under 2 years of age of tuberculous mothers. Infants remain in the institution for a period of one year, practically living in the open air, and their resisting power is materially increased.

TREATMENT

49. Combe: Treatment of Tuberculosis in Infancy with Tuberculin. Le Nourrisson, 1917, **5,** 17.

50. Blumenau, N. R.: Pretuberculosis in Children and Treatment with Tuberculin. Russk. Vrach., 1917, **16,** 289.

51. Hollos, J.: Detection and Treatment of Tuberculosis in Children. Ztschr. f. Tuberk., 1916, **26,** 321.

52. Lasserre, C.: Heliotherapy at Seashore Sanitarium in Southern France. Jour. de méd. de Bordeaux, 1917, **88,** 103.

53. Hyde, C. L., and Grasso, H. L.: Rollier Treatment of Tuberculosis. New York Med. Jour., 1917, **105,** 11.

54. White, W. C., Stewart, A. E., and Shuey, P. F.: New Children's Hospital of the Tuberculosis League of Pittsburgh. Modern Hosp., 1917, **8,** 312.

55. Tilli, P.: Autoserotherapy of Tuberculous Meningitis. Policlinico, Rome, 1916, **23,** 1357.

56. Weil, P. E., and Loiseleur: Treatment of Tuberculous Pericarditis with Insufflation of Air into the Pericardial Sac. Arch. de méd. d. enf., 1917, **20,** 601.

Becker, H. E.: Treatment of Tuberculosis in Children in North Sea Sanitarium. Med. Klin, 1916, **12,** 1353.

Combe[49] believes that tuberculin therapy is only justified in (1) children afflicted with closed tuberculosis or with limited lesions producing a minimum amount of tuberculin; (2) children who produce an insufficient quantity of antibodies, as those with tracheobronchial tuberculosis, and (3) infants whose organisms are not yet adapted to the formation of antibodies. As regards administering the tuberculin, Combe tried the subcutaneous method, but has discarded it because of disastrous results; but he has been very successful with the intercutaneous method. He begins the treatment with an intercutaneous injection of 0.01 mg. of old tuberculin. If the reaction following this amount is less than 5 mm. in diameter, he uses it for the initial therapeutic dose. If the reaction is larger, he commences with 0.002 or 0.001 mg. The injections are given twice a week and the dose doubled at each injection, if conditions warrant. The increase, however, is gaged by the local reaction and the behavior of the eosinophil cells. Progressive diminution in size of the local reaction, as the therapeutic dose of tuberculin is increased, indicates that antibodies are being produced and immunity established, and speaks favorably for the treatment. On the other hand, if the local reaction increases as the dose of tuberculin is increased, the treatment is harmful and should be discontinued. Moreover, in favorable cases there is an increase in the eosinophil cells, which begins two hours after treatment and lasts until the tuberculin is decomposed, so that forty-eight hours after the injection the count becomes normal again. If too large a dose of tuberculin

has been injected, the eosinophilia persists several days, until all the tuberculin is decomposed.

In ten years of experience the author has become convinced of the value of this method, and he has never known an accident to follow the injections. If begun while the disease is still localized, the temperature drops, the appetite improves, the patient takes on weight, and the course, often fatally progressive, is arrested. The method is of no value if the disease has become generalized.

Combe has lately used another agent with apparent success in the treatment of tuberculosis of infants, namely, roentgenography. In the year he treated fifty children suffering from glandular and pulmonary tuberculosis and observed an improvement in their general condition and in the pulmonary lesions as shown by the roentgenograms. The roentgen ray stimulates the formation of connective tissue around the tuberculous lesions. This was proved in one patient who came to necropsy. The child had a tuberculous peritonitis and a lesion in the apex of the lung. The apical lesion had been exposed to the roentgen ray three times at intervals of eight days, and at necropsy it was found arrested and walled in with connective tissue. The thymus gland was found atrophied, and if this was the result of the treatment a word of warning must be sounded, as early atrophy of gland may result in retardation of development.

N. R. Blumenau[50] believes that pretuberculous children should be treated with inunctions of tuberculin. He reports experiments on guinea-pigs which apparently prove that toxins rubbed into the uninjured skin, after it has been shaved and cleansed of grease, pass through the skin as through a special filter and induce the production of antibodies in the organism. The animals kept well and even increased in weight, although they were given inunctions of diphtheria toxin in a 50 per cent. ointment. They then survived the subcutaneous injection of four times the fatal dose of diphtheria toxin. The author's experiments on animals were not numerous, but the results were so convincing that he applied the method at once to seventy children. The most effectual technic was to apply a drop of pure tuberculin to the forearm and then shave off a scrap of skin through it. The mixture of the superficial layer of the epidermis and the tuberculin formed a thin salve-like mixture, which was then rubbed into the skin until dry. Adhesive plaster was applied over the spot. When this was removed twenty-four or forty-eight hours later, the skin underneath displayed a strong, or weak reaction, and the inunction was repeated after an interval corresponding to the strength of the reaction. The dose of tuberculin was also progressively increased to a total of four drops. At first the intervals were usually three or five days, but, when the 4-drop dose was reached, the intervals were a week. The results in

the cases of well defined tuberculosis, especially of the lungs, were, as might be expected, scarcely amenable to treatment, but in incipint or occult tuberculosis the therapeutic results were prompt and striking. Blumenau gives a brief summary of eighteen cases. Some of the children were 9 or 10 months old, but the majority were between 2 and 11 years. Parents usually brought the children to the dispensary because of lassitude, drowsiness and apathy, or the reverse, excessive nervousness and irritability. There was frequently loss of appetite, restless sleep, persistent headache, palpitation, cough, pain in the side or chest and in the bones of the arms and legs. The majority were frail and undernourished. In order to arrive at a diagnosis it is not sufficient only to examine the child, but careful inquiry must be made as to the health of the parents and other relatives to ascertain whether any of them may have had pleurisy or chronic pulmonary disease, or whether any child in the family may have died of meningitis, or any one in the building had a chronic cough. None of the symptoms described are pathognomonic of tuberculosis, but when a possible source of infection is known, Blumenau thinks the tuberculin test will often reveal that they are the results of autointoxication from some tuberculous focus.

J. Hollos[51] emphasizes the importance of detecting latent tuberculosis in children, because he believes that with specific treatment it is in that stage completely curable in a comparatively short time. The symptoms of latent tuberculosis are the result of the toxins on various organs. Especially developmental defects are the result of this tuberculous toxemia. A child who has previously developed normally grows thin and pale, the skin loses its elasticity, the muscles become flabby, the bones are inclined to soften and bend. Digestive disturbances and loss of appetite develop. The child becomes nervous and excitable. He cries easily or is always sleepy. Tuberculous toxins either excite or inhibit the functions of the thyroid gland, so that there may be, on the one hand, vasomotor excitability, rapid pulse, tendency to sweating, and, on the other, stunted growth and mental backwardness. Vasomotor disturbances are very common in children with latent tuberculosis. There is headache, dizziness, irregular pulse, pallor or flushing of the face, cold hands and feet. These children catch cold easily, frequently have eczema and pruritus, pains in the muscles, joints or abdomen. Mental development, however, is usually unaffected. The tuberculous toxins also depress or excite the sexual organs, so that a latent tuberculosis at puberty gives a varied picture. Sometimes there is an early sexual development with profuse menstruation, dysmenorrhea, headache and palpitation. Sometimes menstruation is retarded until the sixteenth or eighteenth year, and then is scant and intermittent. The child grows rapidly but remains pale and weak, and

finally develops the characteristic tuberculous habitus. In boys early and repeated pollutions and sexual nervousness should arouse the suspicion of tuberculosis.

Childhood is the most favorable time to effect a cure of tuberculosis. The process is comparatively recent, retrograde changes and mixed infections have not occurred and lowered the vitality of the organism. Treatment must include (1) prevention of repeated infections; (2) establishment of increased resistance; (3) specific treatment. Under the present social upheaval it is almost impossible to improve social or hygienic conditions and so fulfill the first two requirements. All the more important is the specific treatment, which, according to Hollos, is a positive cure even in poor hygienic surroundings. He regards every infant and every child who lives in a tuberculous environment as infected and advises a course of tuberculin treatment. After eight years' experience with Spengler's I. K. (immune bodies) he is even more satisfied with the results obtained in the treatment of tuberculosis in children than in adults, and not only in latent cases, but in advanced and seemingly hopeless ones. But he has obtained the most beneficial effects from the I. K. in children who have no manifest lesion, only subjective and functional disturbances. Moreover, in these cases the I. K. is a great diagnostic aid, for improvement after injection of small doses (vi to vii dilutions) or after inunctions of medium strength (1:20,000, 1:40,000) establishes their tuberculous nature. A few months' treatment brings about a complete cure. Although individualization in treatment is necessary and close watching is advantageous, Hollos has been able to obtain results by giving injections every three or six weeks and depending on the patient's family to use the inunctions every two or three days. He thinks there is no contraindication for the use of I. K. in the treatment of tuberculosis.

C. Lassarre[52] describes the heliomarine treatment of tuberculosis in children at the Wallenstein foundation. He thinks the wonderful climate of Arcachon associated with heliotherapy is a remarkable therapeutic combination. The foundation has two buildings, the sanatorium and the open air pavilion. The sanatorium is built 500 meters from the water's edge and accommodates forty patients. It has two operating rooms, hydrotherapeutic room, and means for complete radioscopic examination. The open air pavilion has forty beds, twenty for boys between the ages of 4 and 12 years, and twenty for girls between 4 and 18. It is located at the water's edge and is surrounded with pine woods. The routine of treatment is as follows: The children sleep eleven hours, are dressed and exercise in the sand until 8 o'clock, when they have their first meal, of milk or vegetable soup and stew. This is followed by the sun cure and the method of exposure is

practically the same as that of Rollier. At 10 o'clock there are gymnastics; at 11:30 rest in the open air for five hours, interrupted by the midday meal. The evening meal is at 6:30 and consists chiefly of farinaceous foods. Lassarre thinks that the sea baths are an important factor in the treatment. The first bath is given eight or ten days after the child's arrival and they are continued until December, when they are replaced by tepid sprays.

The physiologic effect of the treatment was studied on seventy patients. The pulse is accelerated but always remains full and strong. The blood pressure is diminished during exposure but becomes normal after the treatment. The respiration slightly accelerated. The weight curve always increases. As to the general therapeutic action, the children arrive pale, emaciated and asthenic, and in two months they are completely transformed. The appetite returns, the skin becomes pink, and the children are happy and contented. As regards the local effect of the treatment, the author's experience confirms the opinion of other observers that all local tuberculous lesions are favorably influenced by heliotherapy.

C. L. Hyde and H. L. Grasso[53] describe the Adams Memorial Hospital and the results of the Rollier treatment of tuberculosis obtained there. The plant consists of two pavilions one story high with terraces on all sides 21 feet wide, 12 feet covered and 9 feet uncovered. Each pavilion has a central administration building with a kitchen and dining room in the rear and a wing on either side containing two large wards and four private rooms. For the education of the children two teachers are assigned from the school department. There is a large open air school room used for certain class work and when the weather is inclement. The success of treatment has exceeded the writers' expectation. The effect on the general condition of the patient is most remarkable. There is a rapid disappearance of pain, fever and chills; there is a return of appetite and an increase in body weight and strength and an improvement in the blood conditions. The most characteristic local result in the treatment of tuberculous joints by heliotherapy is the return of motion. There is separation and painless spontaneous expulsion of sequestra and intense recalcification. Sinuses and ulcers discharge more freely at first, sloughing follows and the formation of healthy granulations, and finally, healing. Abscesses are often completely absorbed, as are effusions into the joints, peritoneum and pleurae. Up to date ninety patients have been discharged and there are at present 150 under treatment. The average length of stay at the hospital of all patients discharged was 8.4 months, while the average length of stay for those discharged as apparently recovered was 13.5 months. Of the patients who stayed three months or longer, 67 per cent. were discharged apparently cured or with the disease arrested.

Of those who remained six months or longer, 77 per cent. were discharged apparently recovered, and of those who remained nine months or longer, 82 per cent. were discharged apparently recovered. This shows the importance the length of stay has on the results in surgical tuberculosis. As far as the authors have been able to ascertain, there has been no recurrence of the disease in patients apparently recovered at the time of discharge.

W. G. White, A. E. Stewart and P. F. Shuey[54] describe the new children's building of the Tuberculosis League of Pittsburgh. As one of the chief functions of the Tuberculosis League is teaching undergraduate medical students and nurses, it was necessary to house in this one building many phases of the work. On the ground floor is a ward for fourteen girls and on the second floor a similar ward for boys. On the subbasement floor are the open-air school and toilet rooms, while dining and sewing rooms are on the floor above this. On the dining room floor are the roentgen-ray department and four isolation rooms. On the ground floor with the girls' ward is a small complete operating department, also a students' laboratory, while on the boys' floor is another isolation unit.

P. Tilli[55] reinjected subcutaneously the cerebrospinal fluid obtained by lumbar puncture in three cases of tuberculous meningitis, in children 3 months, 18 months, and 8 years old. In the youngest child the disease subsided and there was an interval of health, but the meningitis returned ten months later and proved fatal. The 8-year-old child recovered and has had no return of the trouble during the three years to date, but the meningitis has caused blindness and the head is much enlarged. The other child recovered completely under the subcutaneous injections of 1, 2 and 3 c.c. of spinal fluid injected every third day. The cure was complete and has been permanent during the two years to date. This is the only case, however, in which no bacteriologic tests were made.

P. E. Weil and Loiseleur,[56] with apparently good results, tried the injection of air into the pericardial sac in a case of pericarditis with effusion. The patient was a boy of 14 years, who in March, 1915, had had an infection called grip, complicated with bronchopneumonia and cardiac weakness. There had been edema of the lower extremities, cyanosis, enlargement of the liver, and ascites. When the writers saw the patient in June, they found signs of pericarditis with effusion and of cardiotuberculous cirrhosis, and a generally precarious condition. On June 2 a pericardial puncture was made and a liter of hemorrhagic fluid withdrawn. This was followed by temporary amelioration of the general condition. On July 11 a second puncture was made, 900 c.c. of seropurulent fluid removed and replaced by 500 c.c. of air. All symptoms quickly disappeared. Again, on the 19th, after the

removal of 300 c.c. of fluid, 300 c.c. of air were injected. The radioscopic examination then showed that the pericarditis had cleared up, but at the upper part of the right border of the heart was a pocket of pus. So a fourth puncture was made under control of the screen and 40 c.c. of fluid withdrawn and the same amount of air injected. On July 26 the child was doing well, had no fever since the second puncture, and could sleep lying down; the pulse was 120, of good quality and the respirations were 32. On August 3 another puncture was made and 300 c.c. of yellow fluid withdrawn and the same quantity of air injected. Then, for an entire month the general condition improved and the fluid did not return. On September 5, however, it was again abundant and a sixth puncture was decided on, when 800 c.c. of fluid were removed and 400 c.c. of air injected. On October 25, in spite of the general good condition of the child, the fluid reappeared, and 750 c.c. of fluid were removed and the same amount of air injected.

The authors insist on the advantage of this method of treatment, which is not painful and does not cause dyspnea or discomfort. The operation is not difficult when the effusion is large, and though very difficult when it is small, it can be performed under fluoroscopic examination with comparative ease. These advantages make it preferable to any surgical procedure for pericarditis with effusion.

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CURRENT PEDIATRIC LITERATURE

ANATOMY AND PHYSIOLOGY

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